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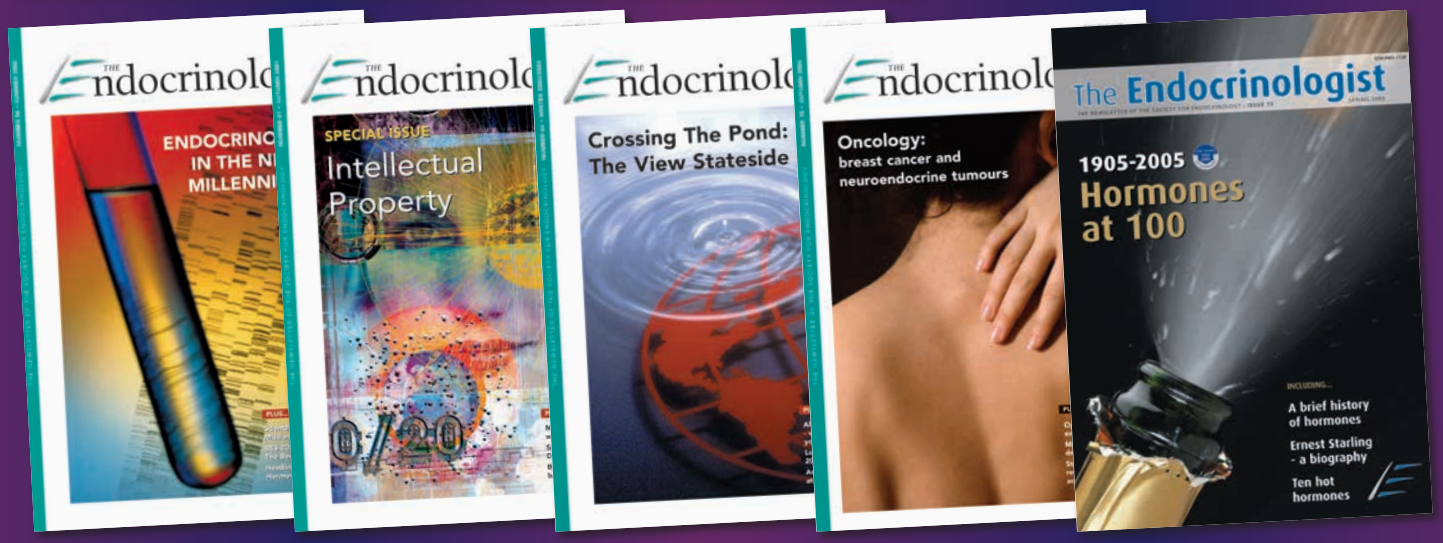
THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY



Browsing through THE ARCHIVES

A word from **THE EDITOR...**

'*Where there is no joy there can be no courage; and without courage all other virtues are useless.*'
Edward Abbey, *Desert Solitaire*, 1968

I saw this quote recently on Twitter and it really resonated for me. The past year or so has been like no other and, whilst I've tried to keep hopeful, at times it has been challenging. I'm an avid data follower – but I have found there is too much data that takes a little bit of hope away.

I realised that, even when things are bad, there are things I can do that give me joy. For me, it is playing tennis (when my Achilles allow it) at my new clay court club, surrounded by trees, hearing the birds and the sounds of cricket and golf balls being hit. Other joys include watching my teenager play cricket, reviewing the progress of my 'crops', hot composting, and hiring and filling a skip with rubbish. Lockdown took away many of the activities we do for fun. Now we can mix again, and this weekend I am going away with my best friend to see the sea – and that will definitely lead to joy.

As we were all a bit busy in March, and recovering from the onslaught that was January/February, this issue has once again had the Editorial Board browsing through the archives. We enjoyed this greatly and, interestingly came up with very similar lists of favourite articles.

They range from describing the first **@hormone_doc**, Ernest Starling (page 31) and the first SfE BES Meeting in 2003 (page 19). On page 8, John Kopchick describes how doing the laundry led to the development of pegvisomant (maybe that 'floordrobe' of mine will lead to something equally profitable!). Open access was topical in 2004, as discussed by Steve Byford on page 22; Adrian Clark gives a 2021 perspective on the same topic (page 24). And as this may or may not be an Olympic year, on page 12, Ian Gallen describes what it takes to keep an elite athlete with diabetes competing at the highest level.

As always, we hope you enjoy reading this issue. Maybe you, like Hotspur who found joy in ResearchGate (page 21), will find a little piece of joy in an unexpected place.

HELEN SIMPSON

Society for Endocrinology
Starling House
1600 Bristol Parkway North
Bristol BS34 8YU, UK
Tel: **01454 642200**
Email: **members@endocrinology.org**
Web: **www.endocrinology.org**
Company Limited by Guarantee
Registered in England No. 349408
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READ THE EDITORS' PICKS FROM *THE ENDOCRINOLOGIST* ARCHIVES

Become a contributor... Contact the Editorial office at **endocrinologist@endocrinology.org**

The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the AUTUMN 2021 issue: **1 July 2021**.

MAKE A DIFFERENCE AT YOUR SOCIETY

Society for Endocrinology 75 YEARS 1946–2021

Have your say and nominate your selection for the vacancy of President-elect on our Council before **17 September 2021**.

We are also looking for a range of members from all career levels, backgrounds, areas of expertise and locations to bring fresh perspectives and new ideas to the following Committees for 2022:

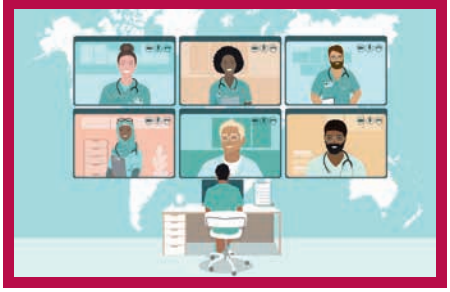
- Clinical (especially members working in district general hospitals)
- Corporate Liaison
- Early Career Steering Group
- Finance
- Nominations
- Nurse
- Programme
- Public Engagement
- Science

If you want represent the Society's members, have a look at the Committee remits and nominate or apply by **1 October 2021**.

You can find full details at **www.endocrinology.org/nominations**.

ONLINE TRAINING OPPORTUNITIES

Our SfE Skills Academy for 2021 is now in full flow, with dedicated webinar series for clinicians, endocrine nurses and researchers. Have you missed any? You can catch up by logging in to the Members' Area of our website. Check the upcoming schedule at **www.endocrinology.org/events**.



THE LATEST IN OBESITY RESEARCH AND PRACTICE

bioscientifica OBESITY UPDATE

Don't miss Obesity Update, an online meeting for professionals and specialists working in the field of bariatrics. It is endorsed by the Society and the Association for the Study of Obesity, and is taking place on 30 June–1 July 2021. Register now at **www.obesityupdate.org**.

ENGAGE YOUR STUDENTS WITH ENDOCRINOLOGY

Apply for the Society's Undergraduate Achievement Award to recognise and promote excellence in the study of endocrinology. Your department could receive £300 per year, for 3 years, to reward outstanding undergraduates for their endocrine-related studies. Applications close on **2 July 2021**. Find out more at **www.endocrinology.org/grants-and-awards**.

REGISTER NOW FOR NATIONAL CLINICAL CASES

National CLINICAL CASES

This virtual event on 22 June 2021 is the ideal forum for trainees to present cases for discussion with clinical colleagues. The ten presented cases will be of interest to the wider endocrine community and will advance understanding of the specialty. Register now to join in: **www.endocrinology.org/events/clinical-cases**.

ADVANCING ENDOCRINE PATIENT CARE

Have you shown commitment to developing and delivering excellent innovative endocrine care? Have you made a significant contribution to the endocrine community and for the benefit of patients? Share your achievements and you could win our Outstanding Clinical Practitioner Award. Apply by **2 July 2021** at **www.endocrinology.org/grants-and-awards/prizes-and-awards/outstanding-clinical-practitioner-award**.

INSPIRING GREAT ENDOCRINE TEACHING

Get some well-deserved recognition in endocrine-related teaching with our 2022 Teaching Achievement Award. This could be for a simple but innovative project, exceptional engagement or a lifetime of sharing your passion. Tell us how you have positively affected learning experiences and attracted students to choose endocrinology. Apply by **2 July 2021** at **www.endocrinology.org/grants-and-awards/prizes-and-awards/teaching-achievement-award**.

REWARDING EXCELLENCE IN ENDOCRINOLOGY

There's still time to make your nominations for our 2022 Medallists: the deadline is **2 July 2021**. Who do you think deserves recognition for their contributions to our field? For more details and to nominate, see **www.endocrinology.org/grants-and-awards/prizes-and-awards/medals**.

SOCIETY CALENDAR

22 June 2021
NATIONAL CLINICAL CASES
Online

17 September 2021
COUNCIL NOMINATIONS DEADLINE

1 October 2021
COMMITTEE APPLICATIONS DEADLINE

8–10 November 2021
SfE BES 2021
Edinburgh, UK

www.endocrinology.org/events for full details

SOCIETY-ENDORSED EVENTS

21–23 June 2021
GUT–BONE AXIS MEETING
Online

30 June–1 July 2021
OBESITY UPDATE
Online

20–21 July 2021
PHYSICAL ACTIVITY AND THE ENDOCRINE SYSTEM
Online

23–24 September 2021
OXFORD ENDOCRINOLOGY MASTERCLASS 2021
Oxford, UK

GRANT AND PRIZE DEADLINES

2 July 2021
SOCIETY MEDAL NOMINATIONS

2 July 2021
OUTSTANDING CLINICAL PRACTITIONER AWARD

2 July 2021
TEACHING ACHIEVEMENT AWARD

2 July 2021
UNDERGRADUATE ACHIEVEMENT AWARD

11 August 2021
TRAVEL GRANT

25 August 2021
SfE BES REGISTRATION GRANT

22 September 2021
PUBLIC ENGAGEMENT GRANT

www.endocrinology.org/grants for full details of all Society grants and prizes

HOT TOPICS

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the Members' Area on the Society website, **www.endocrinology.org**. *Endocrine Connections*, *Endocrinology, Diabetes & Metabolism Case Reports* and *Endocrine Oncology* are open access and free to all. Publishing in *Endocrine Oncology* is currently free.

JOURNAL OF ENDOCRINOLOGY

Obesity, heavy menstruation and delayed endometrial repair

Abnormal uterine bleeding affects 1 in 3 women of reproductive age and is a disorder which is often debilitating. Despite the known impact of obesity on reproductive health, little is known about the effect of obesity on heavy menstrual bleeding.

Reavey *et al.* used a two-pronged approach involving mouse models and human participants to investigate this. From the human study, the authors found that body mass index positively correlated with the extent of menstrual blood loss. To gain mechanistic insight, the authors utilised a mouse model with induced menstrual bleeding and randomisation to a high or a low fat diet. Mice fed a high fat diet showed delayed endometrial repair in comparison with females given a low fat diet. A potential increase in uterine pro-inflammatory mediators was observed.

This may suggest a link between obesity and a pro-inflammatory local endometrial environment, which may affect endometrial repair rate.

Read the full article in *Journal of Endocrinology* **249** 71–82

JOURNAL OF MOLECULAR ENDOCRINOLOGY

Mineralocorticoid receptor signalling in the naked mole-rat

Naked mole-rats (*Heterocephalus glaber*) are mouse-sized rodents with unique physiological features, including exceptional longevity and resistance to age-related diseases. They inhabit subterranean burrows in the arid savannas of North East Africa and are unable to access free water. Control of fluid homeostasis in the naked mole-rat is poorly understood.

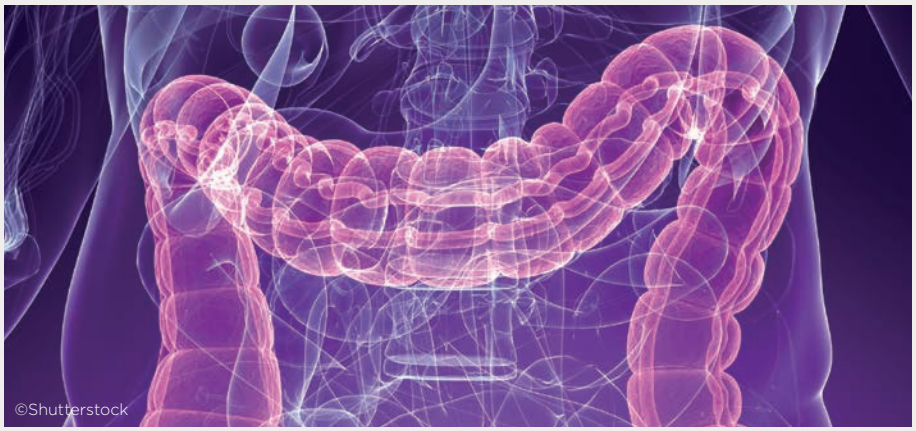
The mineralocorticoid receptor (MR) contributes to fluid homeostasis by modulating sodium balance and blood pressure in response to aldosterone signalling in the kidney. Tetrapods typically carry only one copy of the *MR* gene, but Bactrian camels carry two copies, putatively due to evolutionary adaptation to an arid, desert environment. Although the whole genome of the naked mole-rat has been sequenced, the genomic sequence of *MR* is incomplete.

To investigate how fluid homeostasis is controlled in the naked mole-rat, Oka and colleagues molecularly cloned and analysed the naked mole-rat *MR* gene. They discovered that it is duplicated in naked mole-rats, resulting in two receptors: MR1 and MR2. *MR1* is 90% identical to its mouse orthologue and *MR2* encodes a truncated protein that lacks the DNA- and ligand-binding domains of MR1. In transcriptional activation assays, MR2 alone did not induce reporter gene expression, but co-expression of MR1 and MR2 augmented MR1-dependent transactivation activity in response to corticosteroids.

These results suggest that MR2 functions as a regulator of MR1 activity in naked mole-rats, which may contribute to evolutionary adaptations to control of fluid homeostasis in arid environments.

Read the full article in *Journal of Molecular Endocrinology* **66** 299–311

JOURNAL OF ENDOCRINOLOGY & JOURNAL OF MOLECULAR ENDOCRINOLOGY



Gut Microbiome Special Collection

This joint collaboration by *Journal of Endocrinology* and *Journal of Molecular Endocrinology* presents a fascinating series of review articles showing the increasingly important interactions between the gut microbiome and endocrinology.

This series provides a broad overview of the current literature to date. The review articles cover diverse areas including the regulation and dysregulation of the gut microbiome, endocannabinoids in energy metabolism and metabolic disorders, and how the growth hormone/insulin-like growth factor-1 somatotrophic axis may regulate gut microbiota composition and diversity, with implications for control of growth.

You can read the full articles at **https://joe.bioscientifica.com/page/GutMicrobiome/gut-microbiome-special-collection**

ENDOCRINE-RELATED CANCER

Exercise intensity, inflammation and cancer treatment

Exercise training has been hypothesised to reduce inflammation in patients with cancer. It may be an effective non-pharmacological strategy to limit the impact of inflammation on disease recurrence. Markers of inflammation increase during cancer treatment, but the role of exercise intensity in inflammatory burden has not been explored.

Schauer *et al.* compared the effect of high intensity (HI) versus low-moderate intensity (LMI) exercise on changes in blood inflammatory markers before and after primary (neo-)adjuvant chemotherapy. Patients performed 6 months of combined aerobic and resistance exercise at either HI or LMI. Inflammatory markers were measured in a full cohort of 394 patients with breast, prostate or colorectal cancer, as well as in a subgroup of 154 women with breast cancer. Plasma samples were obtained at baseline, at the end of primary treatment and post-intervention. Regardless of exercise intensity, primary treatment increased inflammation, which was followed by a reduction after cessation of treatment. Interleukin-6 (IL6), IL8 and tumour necrosis factor (TNF) remained elevated after exercise intervention for patients exercising at LMI but not at HI. In patients with breast cancer receiving chemotherapy, C-reactive protein and TNF increased less with HI compared with LMI exercise post-treatment.

These results suggest that HI exercise might protect against increases in inflammatory burden, and patients with breast cancer may benefit from HI exercise during chemotherapy.

Read the full article in *Endocrine-Related Cancer* **28** 191–201

Hot Topics is written by Craig Doig, Douglas Gibson, Louise Hunter, Kim Jonas and Helen Simpson.

CLINICAL ENDOCRINOLOGY

Acute illness in children with secondary adrenal insufficiency

Secondary adrenal insufficiency in children is rare but causes considerable morbidity and, sadly, can result in death. Causes are developmental, such as septo-optic dysplasia, or as a result of treatment of brain/pituitary tumours. A proportion of patients also have learning disabilities.

Rushworth and colleagues describe 47 patients (one with hypothalamic-pituitary-adrenal axis suppression from exogenous steroid). Co-existent cranial diabetes insipidus (CDI) was found in 46% of patients. The cohort had 168 admissions related to adrenal insufficiency/crisis, commoner in those with concomitant CDI. It was found that 60% had prodromal symptoms, 42% of admissions were related to infections, 11.9% had hyponatraemia, 8.9% had hypernatraemia, 10.7% had low blood glucose (<3.5mmol/l). Alarmingly, 20% had a seizure.

This cohort shows how important it is to support patients, their families, and non-endocrinology healthcare professionals with education about sick day rules and adrenal insufficiency. It also shows why, during transition to adult services, patients and their families may have a lot of anxiety about changing healthcare teams. In particular, they may be concerned about moving away from a CNS team who have given a lot of support during the childhood years. We need to ensure we have adult services that 'catch' these vulnerable patients.

Read the full article in *Clinical Endocrinology* **94** 913–919

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Giant bilateral adrenal lipoma in congenital adrenal hyperplasia

Kienitz and colleagues describe the case of a patient with congenital adrenal hyperplasia (CAH) who was found to have bilateral adrenal lipomas. Whilst macronodular hyperplasia and unilateral myelolipomas are seen in people with CAH, this is thought to be the first report of rare adrenal lipomas being found bilaterally.

A 50-year-old man with well-controlled salt-wasting CAH presented with urinary urgency, and breathlessness on bending over. Abdominal imaging detected a 19cm right adrenal mass, and a 11cm mass in the left adrenal. The right-sided lesion was removed at laparotomy, and was found to consist almost entirely of capsulated mature adipose tissue, without histological evidence of malignancy. Although not resected, the left-sided mass had similar characteristics on imaging, and was thus thought also to be an adrenal lipoma.

The authors take the opportunity to discuss more widely the topic of adrenal masses in people with CAH. Routine adrenal imaging is not recommended. It is thought that adrenal myelolipomas might arise due to high adrenocorticotrophin levels, but the pathophysiology underlying adrenal lipomas is unknown.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* doi:10.1530/EDM-20-0204

ENDOCRINE CONNECTIONS

Osteoporosis, sarcopenia and obesity and physical performance in ageing men

Progressive loss of function during ageing occurs with a considerable degree of variability between individuals. This makes assessing each contributing variable challenging. The most common age-related features include reductions in muscle (sarcopenia) and bone mass (osteoporosis), leading to reduced mobility and increased mortality.

Genest *et al.* aimed to examine the influence of these features in combination with obesity. They then specifically related each of them to physical performance in aged males (65–90 years). Examination of 507 participants showed the differential impacts of overall muscle or bone mass. Coincidence of obesity with osteoporosis or sarcopenia was observed in only 15.6% and 2.8% of the subjects respectively, with obesity being the major contributor towards loss of function.

This study suggests that osteoporosis and obesity are more critical determinants of functional decline than a reduced muscle mass. This has potential importance for those studies directly addressing loss of muscle function, encouraging them to account for individual body size and bone mass.

Read the full article in *Endocrine Connections* **10** 256–264.

ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

The number of catalytic cycles in an enzyme's lifetime

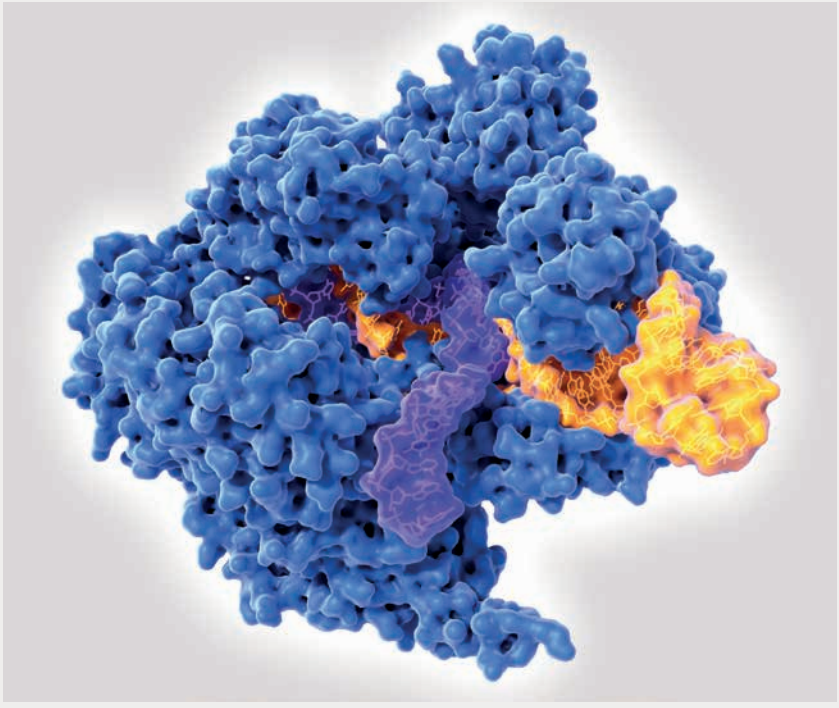
Given optimum conditions, does an enzyme have a set number of catalytic cycles it can perform? Hanson *et al.*, working in the field of synthetic biology, addressed this question by attempting to replicate or, in some cases, even better existing cellular machinery using engineering principles and emerging methodologies.

During manufacturing processes, machined components are optimised to account for failure of parts and the finite properties of materials. In a similar vein, proteins too are perhaps liable to build up accumulative deterioration from chemical insults, such as oxidation. However, the *in vivo* attrition rate of cellular enzymes due to cumulative damage is unrecorded.

This work shows that, unlike manufactured items, enzymes do not experience 'progressive degradation'. Instead, enzymes are liable to instant failure as a result of random catalytic misfire or chemical attack. This suggests enzyme inactivation is more stochastic, although it also follows that the longer an enzyme is around, the more likely it is to experience a random failure event.

Using a series of powerful experiments, the study proposes calculating an enzyme's lifespan using a 'catalytic cycles until replacement' measure. This work shows that it is possible to anticipate an enzyme's functional 'life span', just as could be calculated for a component of a car engine. Using these data, synthetic biologists are able to calculate an enzyme's inherent performance, designing and generating improved versions that can outlast their biological equivalent.

Read the full article in *Proceedings of the National Academy of Sciences of the USA* **118** e2023348118



CRISPR-Cas9: The Cas9 enzyme in complex with RNA (yellow) and single stranded DNA (violet). ©Shutterstock

ENDOCRINOLOGY IN THE NEW MILLENNIUM

WRITTEN BY JOHN R G CHALLIS

FIRST PUBLISHED IN ISSUE 56 (2000)

The general public have never been more interested in healthcare and biomedical research than they are today. There is every reason to anticipate increased public awareness of issues surrounding the effectiveness, availability and costs of healthcare. Because health and healthcare occupy such a central position in the public policy agendas of European and North American countries, it is crucial that, as healthcare investigators and providers, and as an informed lay public, we contribute to the debate.

As biomedical researchers, we should help inform discussion concerning utilization of resources and determination of priorities, and assist in defining the moral and ethical limits of advances in healthcare. Ann Padilla and Ian Gibson (*Nature*, 27 January 2000) remind us that 'scientific knowledge is playing an increasing part in political decision making. Scientists themselves will have to recognize that blind public acceptance of their work cannot be taken for granted. As a consequence, they and their representative bodies will have to examine their roles *per se* and in unfamiliar territory, both political and public'.

Healthcare policy in the new millennium will be dictated by an ability to prevent disease processes, insteading of simply treating them. New genetic techniques, arising in association with the completion of the Human Genome Project, will offer extraordinary new opportunities for partnerships between pharmaceutical companies and academia, in the pursuit of discovery-driven, rather than hypothesis-driven, science. Recognition of epigenetic effects and the role of lifestyle in health performance seem likely to emerge as trends that will influence the spectrum from basic science research to public health policy.

'This research will be driven in part by a requirement to appease shareholders instead of necessarily generating fundamental and new information.'

Healthcare and endocrinology in the new millennium will surely be influenced heavily by demographic shifts. The baby boomers will reach post-retirement age. Their children, the boom echo, having delayed marriage and beginning a family, will emerge with their parents as key public sector groups. Both groups have, in general, been relatively affluent. They will be demanding, vocal and politically active advocates.
It seems inevitable that science itself will undergo a major transition in the way that it is conducted. In Canada, the establishment of the Canadian Institutes of Health Research will see advances being made through a series of virtual institutes. Within these, biomedical and clinical investigators will learn to interact and collaborate with health service/health system investigators, as well as with those interested in population health, and the influences of society, culture and the environment. The use of rapid throughput technologies will see discovery-driven research as a major approach alongside hypothesis-driven activity. Those of us in academia will need to come down from our ivory towers to seek partnerships with colleagues in industry, the private sector and pharmaceutical companies. Although public funding for research in Europe, as in North America, appears ready to increase at a reasonable rate, the high costs of equipment and infrastructure seem likely to require private sector interaction. The lone investigator with the single PCR machine will be stretched to compete independently from genetics-based drug discovery strategies in an industrial setting, with a room full of PCRs running 24 hours a day, 7 days a week. There is no question that this relationship will threaten the integrity of the academic enterprise, and universities will need to rapidly develop policies to ensure that their foundational integrity is not compromised.

In this new paradigm, one might question whether endocrinology will retain a presence as a discrete entity. Already endocrinology itself is largely passé, having given way to paracrine, autocrine and intracrine approaches and explanations. Endocrinologists masquerade as developmental biologists, neuroscientists, cardiovascular physiologists, nutritionists and reproductive biologists. Their studies are crucial to an understanding of the ageing process. We have become the crosscutting glue that joins together other physiologic disciplines. The role of organizations such as the Society for Endocrinology in bringing together workers with a common interest in hormones is crucial to prevent total fragmentation of this discipline into the myriad branches of medicine.

In the new millennium, genes will emerge (if they have not already done so) as big business. The old concept of one gene/one protein is clearly wrong, and the importance of posttranslational modification of protein structure has given birth to the explosion in proteomics. Thus, while genomics leads to characterization and sequence of the genome, and to an understanding of the relationship between gene activity and cell function (functional genomics), proteomics is the mass screen approach to molecular biology. Proteomic technologies aim to document the overall distribution of proteins in cells, characterize individual proteins and elucidate their relationships, interactions and functional roles. New technologies such as microchip arrays, laser capture microdissection, and the application of bioinformatics to two-dimensional gel electrophoresis and interrogation of protein databases will dramatically alter the approach that many of us adopt in conducting our science. Proteomic techniques should lead to new information concerning basic cell function and molecular organization, studies of pathophysiology, genetic and pharmacologic perturbations, and the study of drug modes of action and mechanisms of toxicity. These techniques should lead to the discovery of molecular markers for diagnosis and monitoring of diseases, and the identification of novel biologically active molecules and drug targets.

This research, however, will be driven in part by a requirement to appease shareholders instead of necessarily generating fundamental and new information. Already, pharmaceutical companies are reluctant to develop drugs for diseases that do not have a market, or where the potential of litigation seems likely to threaten or undermine their profit margin. Only the very brave amongst pharmaceutical companies – and clearly there are exceptions – venture freely into the area of drug development for pregnant women, even though premature birth occurs in 10% of pregnancies, accounts for 75% of early neonatal mortality and morbidity, and costs the American healthcare system upwards of $5bn annually. The memory of thalidomide is sadly just too recent when one can more safely seek drug targets in ageing, cancer, AIDS and obesity.

Genomic techniques have led to the rapid development of enormous databases. Fortunately, our national political leaders have recognized

that patent approval for fundamental sequences of the human genome is an impediment to scientific advance, and unethical unless there is clear application and utility of that information. Nevertheless, it seems axiomatic that in the future 'our children will grow up in a world where finding a new gene or protein will be as infrequent as finding, today, a new species of animal' (David Landsman). In a post-genome world, we may envisage complete genotyping of all individuals, a genome-based pharmacology, animal models for every gene, near real-time measurements of gene transcription, and the microdissection of individual cellular processes.

'One senses increasing recognition of the role of the environment as a determinant of health and modifier of gene expression.'

By 2020, one might anticipate that most medical matters will be handled by video or email. Cancer will be treated by anti-angiogenic drugs. Cardiologists will conduct keyhole surgery using robotics over long distances, and will use genetically engineered muscle cells to repair damaged hearts. Hand-held biosensors will monitor blood glucose and pH, and drive artificial pumps in the pancreas to generate insulin, if diabetes itself has not already been eliminated. Each citizen will carry a 'smart card', the size of a credit card, with his or her full genetic code. It will be possible to test the effectiveness of thousands of drugs for that individual in an instant. However, the privacy of that information will require careful preservation. One can imagine prospective employers, potential spouses and exuberant insurance companies demanding a complete medical prediction for each individual entering a new job or relationship.

Jeremy Rifkin, Head of the Foundation for Economic Trends in Washington, DC, has argued that in the new millennium 'animal and human cloning will likely be commonplace with replication increasingly replacing reproduction'. Development of stem cell technology with cloning techniques should allow the generation of specific tissues and/or organs for transplantation purposes. Isolation of genes within individual blastomeres has already allowed prediction of single gene disorders, with genetic diagnosis and gene therapy approaches to treatment or replacement of a defective gene, for example in cystic fibrosis. One predicts that mice will continue to be used in cloning strategies designed to understand basic biologic mechanisms; large animal species will be utilized for practical benefits, and generation of specific proteins. Human cloning will continue to generate moral and philosophical debate, and as scientists we must engage that debate and inform the public and political discussion.

Finally, one senses increasing recognition of the role of the environment as a determinant of health and modifier of gene expression. The studies of David Barker and his colleagues at the University of Southampton have shown clearly that the environment during pregnancy may permanently alter expression of genes in development in a way that determines adult-onset diseases including hypertension and type 2 diabetes. There is an urgent necessity to understand the underlying mechanisms behind this relationship, in order that appropriate scientific information can inform public health policy. In addition, the neutraceutical industry occupies a substantial market – in the USA perhaps $86–$250bn annually. The probiotic market seems likely to have major implications for endocrinology and requires thorough investigation. We need to understand why a population ingests oral extracts of *Ginkgo biloba* to improve alertness and concentration or uses mega-doses of antioxidants to fight disease and restore memory loss. We understand that physical and mental exercise promotes health through enhanced cardiovascular function, prevention of osteoporosis and promotion of neurogenesis, particularly in key hippocampal regions. Appropriate utilization of this information towards a healthy society would be a wonderful advance. In Canada, for example, it was estimated that in 1981 only 20% of the population could be regarded as physically active enough to be considered healthy; this mean number had increased to about 35% by 1995. But, clearly we have a long way to go. Fred Astaire said it best, 'Old age is like everything else, to make a success of it you have to start young'. As we enter the new millennium we have a cacophony of technologies that should allow us to prevent disease and promote good health. We have a wonderful opportunity to ensure that at birth every individual has maximal potential for life-long health. The challenge will be to use that information wisely and in accord with moral and ethical principles that have been debated and deemed acceptable by society at large. Welcome to the new millennium!

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JOHN R G CHALLIS
Chair, Department of Physiology
University of Toronto, Canada
(correct at the time of first publication)

MINI MICE, FOOTBALL AND DIRTY SHORTS

WRITTEN BY JOHN J KOPCHICK

FIRST PUBLISHED IN ISSUE 61 (2001)

What a wonderful molecule! Its ability to cause a decrease in fat but an increase in bone and muscle amazed me. While this might seem rather ordinary to a physiologist, as a molecular biologist, I was hooked! And so, in the early 1980s, I started on my path to try and define the molecular mechanisms of growth hormone (GH) action. I am still on this journey of discovery!

The mid-1980s saw us testing the idea of different molecular 'domains', responsible for GH's various activities, using altered molecules known as 'GH analogues'. We performed classical *in vitro* receptor-binding studies, as structural changes were widely believed to alter a peptide hormone's interactions with its receptor. However, I thought that a cell-based or *in vivo* reporter system would generate additional information – and so transgenic mice came into play. GH transgenic mice possess and express extra copies of GH genes, and are larger than their normal, non-transgenic siblings.

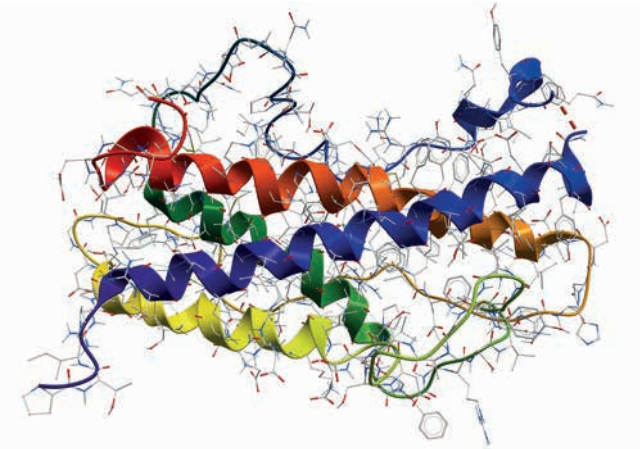
Alongside GH receptor (GHR)-binding studies, conducted using molecules with amino acid substitutions or deletions, we generated transgenic mice expressing the mutated DNA that encoded the GH analogues. We expected that as the *in vitro* binding of the GH analogues to the GHR decreased, there would be a corresponding loss of growth enhancement in the transgenic mice. This was, indeed, the case for many of the GH analogues.

GH contains four α-helices. The third has amphipathic characteristics (i.e. the charged (hydrophilic) and non-polar (hydrophobic) amino acids are separate). However, there is one hydrophilic amino acid amid the hydrophobic residues, and one hydrophobic amino acid and a glycine residue in the hydrophilic area. When we changed these three amino acids to make a 'perfect' amphipathic α-helix, we anticipated an increased potency of GH – a molecule that would bind GHR with higher affinity than native GH, and which would generate 'really big mice'.

However, we found that this 'perfect' GH analogue bound to GHR with the same characteristics as normal GH, and therefore was no more potent than native GH. Our conviction that this perfect third α-helix should possess an altered activity fortunately drove us to generate transgenic mice that expressed this GH analogue. To our surprise, we obtained a small mouse instead of the anticipated giant! We proceeded to show that this molecule was acting as a classic antagonist. This was the first description of a large protein antagonist, and certainly the first GH antagonist.

Changing the three amino acids one at a time showed that only the glycine at position 120 in human GH was important for the activity. Changing this to any amino acid other than alanine resulted in a GH molecule that inhibited growth. Thus one amino acid change out of 191 converted GH from a growth promoter to a growth suppressor or a GH antagonist.

My years in the pharmaceutical industry had 'drilled' into my subconscious that anything that inhibited a physiological process *in vivo* could be of potential value. Long hours in clinical libraries revealed three potential uses for a GH antagonist: acromegaly, diabetic end-organ damage, and certain cancers. Disappointingly, pharmaceutical companies proved unresponsive to a proposal describing our discovery.



Human growth hormone. ©Shutterstock

Physical exercise provided great relief for my frustration. One of the Ohio University football coaches, the late Joe Dean, would routinely ask what I was doing in the lab. It was as we were straining on a weight-lifting machine that I told him about the lack of interest in our potential drug. He relayed to me that one of his former students and football players, Richard Hawkins, knew 'something about drugs'. Rick was founder and CEO of a drug development company called Pharmaco, Inc. Joe scribbled Rick's phone number on a piece of scrap paper and told me I should give him a call. It was by lucky chance that my wife subsequently rescued the very 'clean' piece of paper from our washing machine…

Some days later, while writing an NIH proposal and day dreaming, I decided to call Rick. After an enjoyable conversation, he asked me to send my proposal. Rick subsequently read the proposal during a bout of insomnia, and recounts that he 'could not sleep the remainder of the night'. He was incredibly excited about the GH antagonist and its potential uses, especially for acromegaly. Now, at least, there were two of us!

Together with Rick's friend, John Scarlett, we formed a company, later called Sensus. Here, a small but extremely dedicated and competent group of individuals should be commended for the development of the GH antagonist, along with the many clinicians who performed the clinical trials for acromegalic individuals. The data show that the GH antagonist was efficacious in around 90% of these patients. The FDA is currently reviewing the data. Pharmacia Corp will market the drug, now called Somavert (pegvisomant for injection), if and when it is approved. Hopefully, it will also be tested for other indications, including cancer and diabetic end-organ damage.

So a combination of unanticipated scientific results, coupled with my interest in football, have resulted in a new drug that will benefit many individuals. I would like to acknowledge everyone who has contributed to the discovery and development of GH antagonists, in particular Wen Chen, Nick Okada, Tim Coleman, Joe Dean, Rick Hawkins, John Scarlett, Lawrence and Milton Goll, and Ohio University. This story is dedicated to the memory of Joe Dean.

JOHN J KOPCHICK
Goll–Ohio Professor of Molecular Biology, Ohio University, USA
(correct at the time of first publication)

WHAT EVERY ENDOCRINOLOGIST SHOULD KNOW

FIRST PUBLISHED IN ISSUE 90 (2008)

Interesting tales from the world of comparative endocrinology.

HORSES CAN GET CUSHING'S

Cushing's is found in humans and dogs, but it is also the most common endocrine disorder to affect middle-aged and geriatric horses. It is found so often that some believe it is part of the natural ageing process.

Equine Cushing's syndrome is generally caused by hypertrophy, hyperplasia or adenoma formation in the pituitary gland, although it can also be caused by adrenal tumours. Horses tend to develop pituitary adenomas that originate from the pars intermedia, whereas in humans the adenoma can also originate from the pars distalis. In horses, the most obvious clinical finding is hirsutism (a long coat that fails to shed), but other clinical signs may include polydipsia, polyuria, hyperglycaemia, muscle wastage and laminitis (failure of the bond between the hoof wall and the bone in the foot). The symptoms are controlled through changes in management and/or drug therapy (most commonly with pergolide).

Metabolic syndrome can affect horses as well as humans. Human metabolic syndrome is characterised by obesity, insulin resistance, hypertension and dyslipidaemia. Peripheral Cushing's syndrome or equine metabolic syndrome is characterised by the combination of obesity, insulin resistance and laminitis in mature horses. The effectiveness of insulin signalling at insulin-sensitive target cells is often found to be impaired in native pony breeds, particularly in obese animals, and insulin resistance is thought to be a risk factor for laminitis. It has also been suggested that chronic insulin resistance can predispose an animal to Cushing's syndrome. There is an increasing body of evidence that suggests that certain animals may have a genetic and phenotypic predisposition to the development of equine metabolic syndrome.

LIANE CROWTHER
The Horse Trust *(correct at the time of first publication)*

GROWTH HORMONE BOOSTS COMMERCIAL MILK PRODUCTION

Growth hormone (GH), also known as bovine somatotropin (BST), is used commercially in the USA and elsewhere to increase the milk yield of dairy cows.

The increase is about 10–20%. GH is a homeostatic repartitioning agent, which means it redirects nutrients away from body tissues (adipose tissue and muscle) and towards the mammary gland, where they are synthesised into milk. It works exquisitely to increase the lifespan and synthetic capacity of the milk secretory cells, and the blood flow through the mammary gland, and to reduce the rate of uptake of nutrients at other tissues. The yield-enhancing effects of GH occur within a matter of days. Over a period of weeks, the appetite of the dairy cow is also increased; in the meantime the energy balance of the cow is reduced, such that the additional milk comes from body reserves. GH is administered commercially once every 2 weeks as a slow-release subcutaneous injection.

These effects were first identified before World War Two. Extracting GH from the pituitary glands of culled cattle was considered as a way of increasing the UK's milk supply during the war. But the amount that could be produced in that way would have had a negligible effect on the milk supply of the country. It was the advent of recombinant DNA technology in the 1980s that led to a method of producing copious amounts of GH and enabled its commercialisation during the 1990s.

Use of GH in this way is highly controversial. Its use in the EU and elsewhere is prohibited because of possible (though unlikely) adverse health effects on human consumers of milk, and because of the real adverse health effects it has on the cows. Meta-studies of BST use have shown increased rates of mastitis and lameness in dairy cows, as well as an incidence of infections at the injection site. Even in the USA there are now increased calls for this synthetic hormone to be banned.

MICHAEL ROSE
Aberystwyth University *(correct at the time of first publication)*

SPAWNING SALMON MAY DIE FROM 'CUSHING'S'

With Jamie Oliver on the food revolutionary path again, this time in Rotherham, you may have seen him cajoling novices into creating healthy food in front of a large audience in the town square. Pan-fried salmon was on the menu.

There is little debate that limited intake of salmon and other fish is good for you, as part of a balanced diet. But you may not be so familiar with data from 50 years ago, demonstrating the endocrine mayhem and ill health that the Pacific salmon appears to suffer during migration and spawning.

This amazing fish, the picture of health at sea, migrates hundreds of miles to spawning grounds, only then to die. Post-mortems of spawning fish show very advanced coronary artery disease, and vacuolation of striated muscle. The change in physical appearance from sea to spawning ground is striking, with the appearance of an almost 'buffalo hump' (excuse the cross-species analogy), whilst internally the intra-renal gland increases dramatically. It might not then be such a surprise to find very elevated cortisol levels in the spawning fish. Is the cause of demise Cushing's syndrome? The clinical, anatomical, histological and biochemical data are rather compelling!

JOHN NEWELL-PRICE
University of Sheffield *(correct at the time of first publication)*

HYPERTHYROIDISM IS THE MOST COMMON ENDOCRINOPATHY IN CATS

Feline hyperthyroidism is both clinically and histopathologically very similar to toxic nodular goitre in humans (HTNG). While HTNG is more prevalent in females, the condition affects male and female cats equally. It results in debilitating disease in a significant percentage of middle-aged and older cats.

In both cats and humans, hyperthyroidism is caused by thyrotrophin (TSH)-independent overactivity of one or more benign hyperfunctioning adenomatous thyroid nodules. This leads to high circulating concentrations of thyroxine and tri-iodothyronine, which cause multisystemic clinical signs, including weight loss, increased appetite, tachycardia and polyphagia.

Most HTNG patients exhibit a gain-of-function TSH receptor gene mutation. Many of the receptor gene mutations are directly comparable between feline hyperthyroidism and HTNG. The most common somatic mutation detected in cats (a Met-452>Thr mutation) is analogous to the human Met-453>Thr observed in sporadic human hyperthyroidism.

ANDREW LOWE
From Watson *et al.* 2005, *Journal of Endocrinology* **186** 523–537.

DOGS GET DIABETES TOO

It often surprises our medical colleagues to learn that veterinary surgeons diagnose and treat diabetes in companion animals in much the same way as they do in human patients. Comparative research into diabetes in dogs might offer opportunities that are not possible in rodent models.

Canine diabetes is diagnosed on the basis of clinical signs of polyuria and polydipsia, persistent hyperglycaemia and glucosuria. Virtually all diabetic dogs are insulin-deficient and are dependent upon insulin therapy. It is difficult to use the classification system for human diabetes in dogs, since the underlying cause of the beta cell loss or dysfunction is not usually investigated. However, it is clear that canine diabetes is not a single disease entity and several types of the disease occur.

Neonatal diabetes is seen in particular breeds (primarily Labradors in the UK) but is rare and seems to be due to congenital beta cell aplasia. Most diabetic dogs are diagnosed in middle age (between 5 and 12 years old). Although there is no sex predisposition, female dogs can develop diabetes during dioestrus, which is comparable with human gestational diabetes.

There are clear breed differences in susceptibility to diabetes, with Samoyeds and Tibetan and cairn terriers at an increased risk, whereas golden retrievers, German shepherd dogs and boxers are relatively resistant. This suggests that there is a genetic component to diabetes susceptibility in dogs, and recent work has implicated MHC and some other immune response genes.

There is little evidence that obesity is a major risk factor for diabetes in dogs, which is in contrast to the situation in cats. Thus, canine type 2 diabetes does not seem to exist. Since most dogs suffer from insulin deficiency, it has been suggested that the disease is most similar to the type 1 form of the disease. Although there is evidence for circulating beta cell autoantibodies (primarily against GAD65) in a proportion of diabetic dogs, most are autoantibody-negative. Furthermore, the age of onset suggests that if the beta cell loss is immune-mediated, this process might be more comparable with that seen in latent autoimmune diabetes of the adult (LADA) rather than juvenile-onset type 1A diabetes. Chronic subclinical pancreatitis is also believed to contribute to beta cell loss or dysfunction in some cases.

Much remains to be investigated in terms of the genetic and environmental factors that contribute to canine diabetes susceptibility and the mechanisms that lead to beta cell dysfunction. However, veterinarians aim to contribute to the research effort into this disease, alongside basic science and medical colleagues.

BRIAN CATCHPOLE
Royal Veterinary College, University of London
(correct at the time of first publication)

BIRDS MAY SHOW DEVELOPMENTAL RESPONSES TO STRESS

The long term effects of developmental stress have been studied in mammalian models for many years, to understand not only the underlying mechanisms, but also to determine the consequences for human health

These studies have shown that exposure to glucocorticoid stress hormones during development can permanently alter the reactivity of the hypothalamic-pituitary-adrenal axis. Treatment can also have significant effects on adult behaviour, cognitive ability and important indicators of diseases such as cardiovascular disease and diabetes. However, the continued physiological link between mother and offspring during development constrains the ability to determine the direct effects of stressors on subsequent physiology and behaviour.

Researchers at the University of Glasgow are now using birds to understand the role of glucocorticoid programming in shaping adult phenotypes. Here, there is only a brief window of opportunity for a mother to invest glucocorticoid hormones into each egg, and no direct maternal input of hormones during postnatal development. This therefore allows precise quantification of exposure levels and the scope for controlled experimental manipulation of glucocorticoid levels at several developmental stages.

Although currently in the early stages, this model could provide an important tool in understanding the basic mechanisms underlying the long term effects of developmental stress in humans.

KAREN SPENCER
University of Glasgow *(correct at the time of first publication)*

AN ENDOCRINOLOGIST'S ROLE IN ELITE SPORT

WRITTEN BY IAN GALLEN

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As physicians and endocrinologists, we are used to seeing people with life-threatening endocrine disorders, and to helping people manage the frequently disabling consequences of chronic conditions. However, there are those who have a chronic endocrine disorder, but are at the peak of physical fitness. These unusual individuals require specific support, and we have developed a service to help them manage their endocrine and other disorders and also excel in sports.

MY ARRIVAL IN THE ARENA

My interest in this field was accidental. I had studied the physiology of energy expenditure for my MD, and am a keen, but now failing, rower. In 1997, Steven Redgrave came to see me to discuss his then newly diagnosed diabetes. Steven was preparing for his fifth Olympic Games, this time rowing in the 'coxless fours' event. Steven was sceptical but pleased to hear that I believed that, with careful management, he could return to maximal physical performance, and be able to compete at the 2000 Olympic Games. I believed that this might be possible because Steven had extensive pre-diabetes physiological studies which would provide a unique baseline to work from, and because short-acting analogue insulin had recently been introduced.

TEETHING PROBLEMS

The initial period of conventional diabetic management was a failure, with Steven complaining of very low levels of energy and work output, and suffering frequent episodes of hypoglycaemia on the water. We decided to return Steven to his successful pre-diagnosis food intake and training programme, and to manage his diabetes around the 6,500–7,000 calorie diet of high glycaemic index foods. This would require the development of an unusual multiple daily insulin injection regime. To maintain glycaemic control avoiding hypoglycaemia required five or six injections of analogue insulin per day, each at a very small dose, and two unusually timed basal insulin doses.

Initial progress was swift, but further issues were identified following high energy expenditure rowing events. Again, physiological studies were essential to identify problems with refeeding and energy storage. Further refinement of this regime enabled specific refeeding programmes to normalise Steven's work output to close to that seen before diagnosis of diabetes.[1]

FINE TUNING

In the preparation for the Olympic Games, every potential rowing eventuality, such as delayed start of racing, repechage (additional races for qualification) or multiple races in a day, was considered and the appropriate response practised. The iconic video image of the race and Steven's celebrations has been voted as our outstanding sporting achievement.

As a result of the publicity following Steven's success, young sportsmen with diabetes asked to see us to help in their management. Over the following decade, we have found that patients attending the service complain of three main groups of symptoms:

- seemingly inexplicable dysglycaemia during and immediately following exercise
- unexpected and severe hypoglycaemia, particularly at night
- excessive fatigue, impaired physical performance and increased muscle weakness and cramps when compared with their prediabetic state or with peers (this is probably the most subtle of the three groups of symptoms).

To deal with these issues, we aim to reduce day-to-day variation in insulin therapy technique and to improve insulin dosage relative to carbohydrate intake. A focus on detail is extremely important, as we frequently find that much of the apparently inexplicable variation in glycaemic control is not due to exercise but due to these factors. A detailed history of the sporting/exercise programme is made. Particular attention is paid to the timing, duration, intensity and type of exercise on each day of the week. This allows the exercise to be characterised so that the anticipated effect on blood glucose levels can be identified. In general, the exercise is classified as endurance (in which case blood glucose can be predicted to fall), high

intensity (where blood glucose is likely to rise) or mixed exercise, such as team sports, where the effect may be variable from day to day, depending on the intensity of each event (although the general effect tends to be a fall in blood glucose levels which is attenuated when compared with pure endurance exercise).

Importantly, the timing of each event in relation to the bolus dose of insulin is identified, as well as any adjustments which are made to this dose. Particular care and attention are paid to symptoms suggestive of hypoglycaemic unawareness. Severe hypoglycaemia in young adults who are sleeping on their own is of special concern, and where found requires specific attention. Listening to what those young people had to tell us has led to practical recommendations for managing different sporting activities.[2] The experience of our patients is also disseminated though our website (**www.runsweet.com**) and its forum.

ACADEMIC PERSPECTIVE

There was, however, a significant lack of scientific evidence underlying this clinical field. Steven Redgrave's experience spurred on our investigations and those of others in this area, and we now have good evidence of the metabolic and endocrine effects of insulin-treated diabetes on risks and avoidance of hypoglycaemia, and on how to optimise insulin and continuous insulin infusion therapy.[3,4]

We understand the hormonal and metabolic responses to exercise, how these responses are altered by type 1 diabetes and insulin therapy, and how a number of endocrine disturbances can influence glucose regulation during exercise, making the management of glycaemia challenging for patient and caregiver. We have seen how increased insulin sensitivity and the reduction in counter regulatory hormone response to hypoglycaemia seen following exercise, particularly in men, may predispose to severe nocturnal hypoglycaemia. There remains a lot more to understand.

Our particular interest is managing perceived impairment in physical performance in diabetes, but we have been asked to review athletes without diabetes, who have performed well, but who are currently off the pace. Such impairment of performance is frequently attributed to a 'post-viral' condition. This has lead to a further, very interesting area of development. We are able to study these young people in our well equipped exercise laboratory and, following a standardised exercise programme to exhaustion, we can monitor gas exchange, electrolytes and intermediary fuels. In the cases we have studied, we have found interesting variation of glucose metabolism, alteration in fuel utilisation and variation in electrolyte fluxes at maximum performance which have responded to treatment.

THE FUTURE

The merging of endocrinology, physiology and metabolism provides a fascinating clinical experience and an exciting new area for translational clinical research. For the athletes, it offers the promise of a return to optimal performance. The prospect of the Olympics coming to London provides a good springboard for the UK to be at the forefront of this area.

IAN GALLEN

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HOW ARE HORMONES MEASURED? A JOURNEY IN ENDOCRINOLOGY

WRITTEN BY JULIAN H BARTH

FIRST PUBLISHED IN ISSUE 111 (2014)

Hormones have been measured by immunoassay for more than four decades, since Berson and Yalow discovered that antibodies could be used as diagnostic agents. They were awarded a Nobel Prize and, altruistically, did not patent their findings.

However, the story of hormone assays begins earlier, with a variety of *in vivo* biological tests. Subsequently, colourimetric assays were discovered and used to good effect, particularly for cortisol. Since 1970, immunoassays have become increasingly routine and, after a period of dominance within the clinical laboratory, it is only now after a further 40 years that a new technology, tandem mass spectrometry (TMS), is starting to emerge as the method of choice.

EARLY TESTS USING BIOLOGICAL EFFECTS OF HORMONES – BIOASSAYS

The early bioassays included the chick cockscomb test. Androgen-like material was applied to the cockscomb of a chick, and the increase in size was used as a measure of testosterone. One can only imagine the errors that might have been introduced while trying to hold the animal still in front of a lamp, whilst the shadow of the comb was outlined on a screen to measure its size.

Another qualitative test used the *Xenopus* toad, which ovulated in response to human chorionic gonadotrophin injections, and was used as an early pregnancy test. Probably more precise was the ovarian weight augmentation assay in immature rodents, used to measure follicle-stimulating hormone (FSH).

DEVELOPMENT OF MODERN IMMUNOASSAYS

Early immunoassays using antibodies from immunised animals with ^{125}I-labelled hormones in competitive assays were very welcome. These assays were time-consuming. In the 1970s, luteinising hormone and FSH

Technicians at a NHS laboratory in the 1950s carry out pregnancy tests using *Xenopus* toads. Reproduced by kind permission of Audrey Peattie

assays took 5 days, from pipetting the samples on a Monday through to calculation and reporting of results on a Friday, but by the late 1980s a batch of 30 samples could be measured in a day.

In those days, the assays were all built in-house, and our older colleagues will remember the 'hot labs' where they iodinated their ligands, and the local university animal house where they venesected animals for their polyvalent antibodies. I remember being regaled with tales of a colleague being flung skyward at the university farm by an angry ram who was in no mood to donate his blood to science.

The antibodies were not always very precise in their detection of specific molecules, hence preparatory separation of serum samples was required, using techniques such as paper and column chromatography or organic solvent extraction to increase the specificity of the antigen available to be bound. These methods are very time-consuming and require considerable technical skill. This issue of specificity was addressed by the next milestones.

BENEFICIAL REFINEMENTS

First we saw the development of monoclonal antibody production from hybridomas (associated with another Nobel Prize). Secondly there was the development of non-isotopic labels, such as enzymes, luminescence, delayed fluorescence, polarisation fluorescence etc. Thirdly we benefited from the merging of biological with mechanical sciences as robotic instruments were developed. These instruments can pipette faster and more precisely than humans and, equally importantly, could ensure that incubations were precisely timed, so that assay numbers could be increased from 30 per day to several hundred per day without any assay drift across batches.

The increase in productivity comes with a cost. Direct assays for steroid molecules are still prone to interference from other molecules. Monoclonal antibody kits from different commercial providers are proprietary agents, and so there are variations between methods that persist even with international reference preparations. Moreover, monoclonal antibodies may not necessarily be the best tool for measuring peptide hormones that exist with many glycoforms and oligomeric forms.

Immunoassays have developed outside the clinical and research laboratory environment and are now used by clinical staff as near patient tests, by field toxicologists for environmental poisons, and by the lay public as pregnancy and HIV tests.

The existence of interference by molecules similar to the ones under investigation has already been mentioned but, over the years, every time an assay for a novel analyte has been produced, it has been followed by reports of antibody interference. These are usually only noted when assay results clearly diverge from the clinical picture, but our group has shown that more subtle interference occurs in at least 1:200 patient samples. The interference is quite promiscuous and not limited to a single analyte.

TANDEM MASS SPECTROMETRY – THE FUTURE?

The scaling down of mass spectrometers from the size of a double bedroom to a desk top instrument has permitted the introduction of this technology to the clinical laboratory. TMS using quadrupoles is only useful for the measurement of small molecules such as steroids, drugs and intermediary metabolites, and more sophisticated instruments are necessary for peptide hormone measurement. It is remarkable that, despite it being less than 10 years since the first reports of the use of TMS in endocrinology, *Journal of Clinical Endocrinology & Metabolism* has stated that it will only accept papers that use TMS methods for steroid analysis in future.

'Endocrinology has developed in tandem with immunoassays, and both sciences have progressed in leaps and bounds since the seminal work of Berson and Yalow in 1959. The next game changer will be the analysis of hormones in real time by the patient.'

TMS is presently a sophisticated technique that needs skilled staff, but it will undoubtedly become a more friendly technique in the future. After all, mass spectrometry is used in airport security for the detection of volatile explosives, so it is only time before this comes to routine clinical laboratories. Inevitably, as TMS is more widely used, newer types of analytical problem will be found. We are already aware of interference by substances that co-elute in the preparatory columns and by epimers and structural isomers. So watch this space…

Endocrinology has developed in tandem with immunoassays, and both sciences have progressed in leaps and bounds since the seminal work of Berson and Yalow in 1959. The next game changer will be the analysis of hormones in real time by the patient.

JULIAN H BARTH
Consultant Chemical Pathologist, University of Leeds
(correct at the time of first publication)

OUT OF THE CLINIC AND INTO THE LAB: A STRATEGY FOR SURVIVAL

WRITTEN BY ANNA CROWN

FIRST PUBLISHED IN ISSUE 55 (2000)

This article is based on Anna Crown's very well-received talk entitled 'PhDs/MDs and how to survive them', given during the 190th Meeting of Society in November 1999, as part of the Young Endocrinologists Symposium.

My aim is to help medics embarking on laboratory-based research. My own experience, and my observations of medics in the lab, form the basis of this article. Perhaps the most important advice is that you should only undertake research if you want to; to do it because you think you should is a recipe for misery and disaster.

The laboratory has a pyramidal hierarchy, from professors at the top, through senior lecturers and lecturers, to post-docs (who have completed their PhD theses, and are the equivalent of SHOs or SpRs), to PhD and BSc students. Technicians are also an integral part of the lab, and by no means necessarily at the bottom of the pyramid. Unlike the 3- to 6-month jobs of many junior doctors, the contracts of lab staff are usually 1–3 or more years long. Sensitivity to the interpersonal dynamics of the lab you join is vital. Unfortunately, on your first day, you cannot necessarily expect people to regard you neutrally. They may have had bad experiences of previous medics in the lab. You are probably being paid more than a scientist of equivalent seniority, as you embark on work for which you will be seen as almost totally untrained.

It is vital that you appreciate quickly how much you have to learn. If your most recent lab experience is A-level chemistry, effectively you know nothing. You will have to be taught how to weigh chemicals, how to use a pipette, how to make up solutions and so on. If you are too arrogant to learn these basics properly your experiments are bound to fail. Don't assume that you can extrapolate from your medical or surgical experience of sterile technique to a cell culture hood without explicit instruction. There is plenty of scope here to ruin both your own experiments and those of others. It is hard to recover from that sort of unpopularity. Be humble, and get someone friendly to show you how it all works! In the early stages, it is also good to ask somebody to check your experimental designs, to be sure you have included appropriate controls and to avoid unnecessary frustrations. Although you are used to working independently, your lab work will need fairly close supervision to start with. Remember that no-one is there to set up or finish off your experiments. This includes routine work like looking after your cells in culture, and menial tasks like washing up. It is simply unacceptable to be 'bleeped away' half way through something. Later, when you are competent to reciprocate, there may be scope for some give and take. Do not become the flatmate from hell, leaving the sink full of washing up, finishing off chemicals, or leaving radioactive waste lying around for someone else to dispose of! I have also observed that gory 'Doctors' Mess' talk does not usually go down well in laboratories; scientists, sensibly, do not see the funny side of patients being found dead on the toilet.

'It is vital that you appreciate quickly how much you have to learn. If your most recent lab experience is A-level chemistry, effectively you know nothing.'

My last 'negative' point: remember that there is often a period of despondency shortly after you start your research. You move from a busy schedule to an apparently empty one. It takes time to get going, and even longer to get results. Scientific research lacks the immediacy of clinical medicine. You don't get the instant gratification of making someone better. Conversely, if a technique is not working, it won't go to ITU or die, so you just have to tussle with it.

Moving on to the positive side of the transition. Get fully involved in the lab – enjoy it! Go to lab meetings and journal clubs, and don't chicken out of presenting genuinely 'scientific' papers, including the 'Methods' sections! Abandon the Doctors' Mess and go to the lab tearoom instead. Here you can get to know people. Labs can be really friendly; you may even get a birthday cake and a card if you're lucky – something I have never known to happen on the wards! If things are slow to get going, turn this to your advantage. Use your spare time to get acquainted with the relevant literature. Improve your IT skills. Do a statistics course. Most grants allow for one clinical session a week. If you do not have to provide a service commitment, you can take advantage of your uncluttered timetable to attend speciality clinics that interest you. I would, however, suggest that other than this one session, and the occasional acute medical take, you should abandon clinical work completely if possible whilst doing your thesis.

There are many other ways to enhance your research experience. It is useful to make contacts both locally and elsewhere. Find out who is doing similar or related work, seek advice, and set up collaborations. Get involved in 'off-shoot' projects which may well be productive in unforeseen ways. Attend meetings, submit abstracts, present posters and give talks.

Remember that as a clinician there are small ways in which you can be helpful in the lab! Biomedical scientists like to set things in clinical contexts, so you may be called on for thumbnail sketches of diseases. Perhaps you can see potential clinical applications of work that have not previously been considered. You may be used to provide a phlebotomy service or to gain access to other human material. Your personal clinical advice may even be sought, or you may be needed for first aid. You are bound to be taking a lot from your lab; it makes sense to take up any opportunities to reciprocate.

The return journey to the wards can also be difficult. Facts that used to be at your fingertips seem to be lurking somewhere in your mid-brain. Friendly, familiar faces who you relied on for favours may have moved on. The challenge is increased if you are trying to combine research with continued clinical training, under the new Calman regimen. My only definite recommendation is that you try to finish writing your thesis before you return to the wards. It is much more difficult to squeeze it in afterwards.

Finally, I would suggest that you will optimise your research training if you have both a scientific and a clinical mentor. As I was told early on in my research, it is all too easy as a clinician scientist to impress scientists with your clinical acumen and clinical colleagues with your scientific genius, whereas one's aim should be to be respected by scientists as a scientist and by clinicians as a clinician.

ANNA CROWN
Bristol Royal Infirmary *(correct at the time of first publication)*

PPI: ITS IMPORTANCE IN THE DEVELOPMENT OF RESEARCH

WRITTEN BY ANNE MARLAND

FIRST PUBLISHED IN ISSUE 127 (2018)

Hopefully, everyone reading this article is familiar with PPI: not insurance which has potentially been mis-sold, but rather 'patient and public involvement'!

Humour aside, PPI is one of the most important factors influencing the development of research and, for most of us, affecting our successful delivery of metabolic and endocrine findings.

Good PPI improves the quality of research. Patients and the public can be involved in many ways, including helping to design research, making sure the research is relevant, advising on which research should be funded and reviewing project applications.

UNDERSTANDING INVOLVEMENT

INVOLVE is part of the National Institute for Health Research (NIHR). It defines public involvement in research as 'Research being carried out "with" or "by" members of the public rather than "to", "about" or "for" them. This includes, for example, working with research funders to prioritise research, offering advice as members of a project steering group, commenting on and developing research materials and undertaking interviews with research participants.'

INVOLVE uses the following terms to break down the activities.

Involvement

This is where members of the public are actively involved in research projects and in research organisations. Examples of public involvement include people taking part:

- as joint grant holders or co-applicants on a research project
- in identifying research priorities
- as members of a project advisory or steering group
- in commenting on and developing patient information leaflets or other research materials
- in undertaking interviews with research participants
- as user and/or carer researchers carrying out the research.

Participation

This is where people take part in a research study. Examples of participation are people joining in:

- as recruits to a clinical trial or other research study, to take part in the research
- to complete a questionnaire or participate in a focus group as part of a research study.

Engagement

In this case, information and knowledge about research are provided and disseminated. Examples of engagement are:

- science festivals open to the public with debates and discussions on research
- an open day at a research centre where members of the public are invited to find out about research
- raising awareness of research through media such as television, newspapers and social media
- disseminating the findings of a study to research participants, colleagues or members of the public.

HOW TO INVOLVE OTHERS IN YOUR RESEARCH

Hopefully most of you will be involved in some aspect of research – or maybe it's an area which you and colleagues in your department wish to explore. You have probably already considered why you want to involve the public or patients, and who you want to involve.

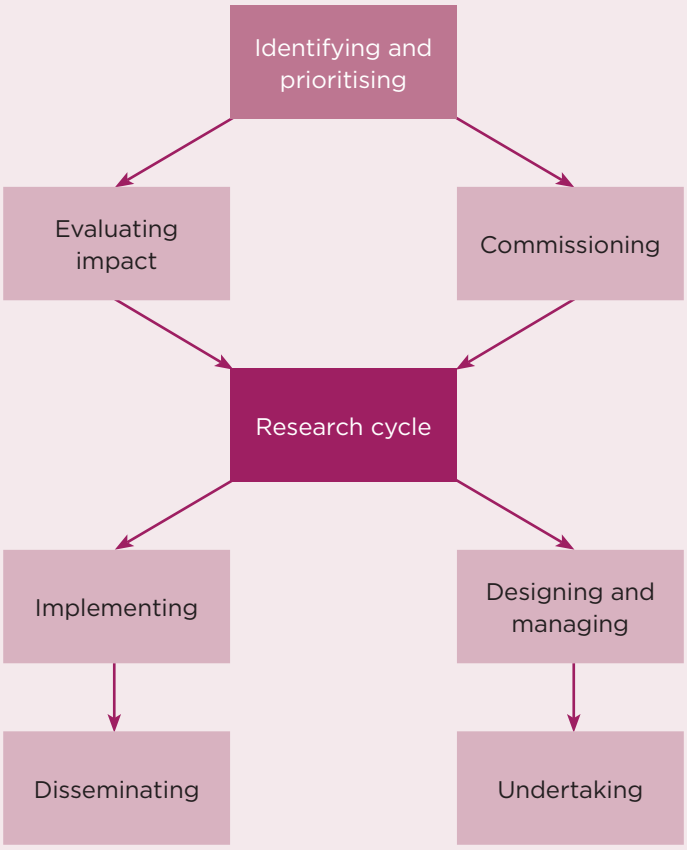
You now need to consider how these people are going to be involved in the different stages of the research cycle.

Nurses are perfectly positioned to play an important role in the process of involvement. We recognise and value the involvement of patients and the public in research. Nurses have excellent, advanced communication skills which demonstrate a desire to listen, understand and help with any question which may arise during an opportunity to discuss research with patients or the public. This establishes a therapeutic relationship with patients and the public with unconditional positive regard.

Within the context of the multidisciplinary research team, we offer a different perspective, where discussions with colleagues will help to alleviate 'jargon' and allow barriers to communication to be reviewed and addressed. Nurses act as the hub of communication, relaying and interpreting information between doctors, patients and carers. This ability provides the best possible outcomes for successful recruitment and involvement in research.

For many, the process will involve organising a meeting, for example, for project advisory groups, public events, reference groups or workshops. How you plan these meetings can make a huge difference to how people feel about the research and how much they are able and want to get involved in your work. Holding a meeting is only one of the ways to involve people, and you may decide that this is not the best approach for your research. There are many other ways of involving patients and the public in research (see **www.involve.nihr.ac.uk**).

The research cycle. ©Anne Marland



WHAT TO CONSIDER WHEN ORGANISING MEETINGS

There are several factors that can aid your meeting's success.

- Explore opportunities for meeting patients or the public in their own environment, for example by attending a regular meeting of an organisation or group.
- Consider venues that are on neutral ground.
- Organise meetings at times and in places that make it easy for people to attend. Those who are working, have young children or are carers might need to meet outside office hours.
- Make sure that there is parking and public transport nearby.
- It may be better to plan for a mid-morning or early afternoon start to the meeting. This makes it easier for people if they have to travel some distance to attend or if they need additional time in the mornings because of their disability or health condition.
- Make sure meeting places, hotels and facilities are accessible to all those attending; for example, if you are inviting a wheelchair user to join your committee, meet in an accessible meeting room with parking nearby and fully accessible facilities.
- Where possible, visit the venue in person in advance of the meeting, and ask to be shown around to check its suitability and the access to all rooms, such as the dining area and disabled toilets. Don't rely on the venue telling you that it is accessible, as you might find that this is not the case or that the complex routes of access are not acceptable to the people needing access.

RUNNING THE MEETING

How the meeting is conducted is very important. Agree ground rules for how you will manage the meeting, so everybody has an equal opportunity to contribute. A Chair is necessary to keep balance and control. It is important that all group members, including members of the public, agree to these rules of mutual respect. Make sure that everybody has an equal voice in the group.

It is essential to encourage the use of clear language, and to explain jargon and acronyms. You should ask the Chair to check regularly that people understand the language used and the content of the meeting.

Frequent breaks and refreshments are important, as people might need to take medication or find sitting for long periods difficult. If it is possible to have a spare room, then allocate this as a quiet room for those who might need to take some time out of the meeting.

To allow people the opportunity to contribute in different ways, you might consider different ways of conducting meetings: for example, time in small group sessions, as well as meetings in a larger group. A mentor or buddy system can be useful to support the members of the public you are involving on an ongoing basis.

I hope reading this article will encourage you to involve PPI in your clinical setting, and that you can see how valuable it is to involve nurses, because of our skills related to all aspects of this approach. Our responsibility as nurses to the development and support of research is essential, and we can all make a difference.

ANNE MARLAND
PPI Nurse Representative for the NIHR Metabolic and Endocrine Specialty UK Group; Advanced Nurse Practitioner in Endocrinology, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford University Hospitals NHS Foundation Trust
(correct at the time of first publication)

Society for Endocrinology
1946–2021
75 YEARS

We can't wait TO SEE YOU

Join us in Edinburgh this November for the long-awaited return of SfE BES 2021. This year marks our 75th anniversary, and we can't wait to get together to celebrate our achievements, and look forward to our future.

The Programme Committee has once again developed an exciting and inspiring programme, featuring the latest world-class science, clinical best practice and innovations from our field.

This year's conference will include our **75TH ANNIVERSARY LECTURE**, delivered by **Dr Jeffrey Friedman**, renowned for his discovery of leptin. We are also excited to welcome **Professor Sir Peter Ratcliffe**, winner of the Nobel Prize for Physiology or Medicine in 2019, who will be delivering our **PRESIDENTIAL LECTURE**.

We are working to bring you digital content to complement your attendance, and support those colleagues unable to travel.

This year's conference promises to be a celebration of our community and offers us a chance to reconnect after the challenges of the past year. We can't wait to welcome you back to the UK home of endocrinology.

SfE BES 2021 PLENARY LECTURES:

DALE MEDAL LECTURE
Professor Sadaf Farooqi (Addenbrooke's Hospital, Cambridge)

JUBILEE MEDAL LECTURE
Professor Stephen Shalet (University of Manchester)

SOCIETY FOR ENDOCRINOLOGY MEDAL LECTURE
Professor Jeremy Tomlinson (University of Oxford)

STARLING MEDAL LECTURE
Professor Roland Stimson (University of Edinburgh)

INTERNATIONAL MEDAL LECTURE
Professor Mark Febbraio (Monash University, Melbourne)

TRANSATLANTIC MEDAL LECTURE
Professor David D Moore (Baylor College of Medicine, Texas)

EUROPEAN MEDAL LECTURE
Professor Greet Van den Berghe (University Hospitals, Leuven)

CLINICAL ENDOCRINOLOGY TRUST LECTURE
Professor Márta Korbonits (Queen Mary University of London)

CET VISITING PROFESSOR LECTURE
Professor Gary Hammer (University of Michigan Rogel Cancer Center)

BRITISH THYROID ASSOCIATION PITT-RIVERS LECTURE
Professor Heike Heuer (Universitätsklinikum Essen)

Abstract submission is open! Deadline **Monday 5 July (11:59pm)**

Register or submit your abstract at **www.endocrinology.org/sfebes2021**

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BES: IN THE BEGINNING...

WRITTEN BY COLIN BEARDWELL

FIRST PUBLISHED IN ISSUE 66 (2003)

Every spring, hundreds of endocrinologists gather together for 3 days to absorb new facts, gather ideas for research and socialise with old friends. Then they all return home and settle down to work for another year, until the following spring when they repeat the same thing all over again. Though certainly a well-loved ritual, it is difficult to believe that meetings of the BES only date back 20 years. How and why they came into being has already started to fade into the mists of time.

Endocrinology changed dramatically between 1960 and 1980, a period when my contemporaries and I were mostly training or had just become consultants. The clinical endocrinology of the 1950s was largely descriptive. The symptoms of many endocrine disorders had been recognised, but few hormone assays were available or accurate. Peptide hormones could not be measured at anything like physiological concentrations, and individual steroids could only be measured by isotope dilution after isolation by days of paper chromatography. We were consequently ignorant of most things that are now taken for granted.

After 1960, the introduction of radioimmunoassays, the rapid advances in cell biology and biochemistry and the development of computed tomography and magnetic resonance scanning made endocrinology one of the most rapidly advancing and fascinating fields of medicine and basic science. These advances attracted many highly intelligent graduates; existing endocrine units expanded rapidly and new units developed across the country.

'BES meetings have certainly served to meet the key objective of their original organisers – to promote the international reputation of British endocrinology!'

The traditional means of exchanging information came under increasing strain. The twice-yearly meetings of the Society for Endocrinology were largely devoted to basic science, the Endocrine Section of the Royal Society of Medicine (RSM) met monthly and catered for clinical presentations, while smaller, specialist societies such as the Thyroid Club, the Bone and Tooth Society, the Ovarian Club and the Hormone Section of the Biochemical Society dealt with special interests. These were the main meetings for the presentation of endocrine data. Most took place in London, presenting difficulties for the increasing numbers who worked elsewhere. Anyone who wanted a broad overview of British endocrinology needed to subscribe to a bewildering variety of societies, some of which were not accessible to juniors.

For all these reasons, and because many of us had enjoyed the International Congresses of Endocrinology, the 2-yearly *Acta Endocrinologica* meetings in Europe and the Endocrine Society meetings in the USA, my contemporaries and I favoured a single, big annual meeting in the UK, to cover the whole field. But we had to convince those senior to us of the need for change.

Our seniors were in all the positions of power on the important committees. They too were affected by the rapid changes in the field, but also had a medicopolitical agenda. British endocrinology had made great advances, but they felt that it hadn't received the recognition that it deserved overseas. Those who were already convinced of the need for a new national annual forum also saw it as an opportunity to increase the worldwide influence of British endocrinology. From 1970 onwards, moves to strengthen international ties were made.

One of the foremost problems was British representation on the committee of the International Society of Endocrinology, which was responsible for the 4-yearly International Congresses. The number of representatives from each country depended upon the size of the national endocrine society. But which of the plethora of British societies should be approached for nominations and how many representatives should there be? To try and provide some unity, a Liaison Committee with representatives from the two main societies was established, and in 1975 the British Diabetic Association was also invited to join.

Moves were also being made to broaden and improve the standard of scientific presentations at the Society for Endocrinology's spring meetings. In 1978, the then Chairman, Roger Short, suggested that it should become more like a symposium, with two or three major lectures, that some of the meetings should be held outside London, and that the Endocrine Society should be approached with a view to establishing transatlantic lectureships.

These ideas were favourably received and further developed informally, until, at a meeting of the Liaison Committee in October 1980, it was suggested that a loose federation of British endocrine societies should be formed, with a view to holding an annual general endocrine meeting. The proponents of this scheme seem to have included Lesley Rees, Vivian James, David London and John Phillips, as well as Roger Short from the Society for Endocrinology, and Michael Besser, Chris Edwards and David Heath from the RSM.

In May 1981, at a meeting with representatives from several of the specialist endocrine societies and the Irish Endocrine Society, it was agreed to form a new Liaison Committee, tasked with the organisation of an annual meeting of British Endocrine Societies (BES). Some of the societies feared loss of their individuality. On this basis, the British Diabetic Association decided to hold its own meeting, but on the same site and immediately following the BES, with a joint symposium linking the two meetings. Likewise, the Thyroid Club chose to hold its own meeting within the BES, though open to all, and including the annual Pitt-Rivers Lecture.

The British Endocrine Federation was recognised by the International Society for Endocrinology, and so achieved the other aim of allowing full representation on that body.

From these beginnings, the annual BES meetings have gone from strength to strength. The scientific standard has remained exceptionally high, other societies have joined in, and overseas representation has increased. Above all, the BES meetings have certainly served to meet the key objective of their original organisers – to promote the international reputation of British endocrinology!

COLIN BEARDWELL

I am very grateful to all who have helped compile this record in response to my queries: Lesley Rees, Clara Lowy, Howard Jacobs, Roger Short, Michael Besser, David London and Vivian James.

STEPS TO A FELLOWSHIP

WRITTEN BY DAVID RAY & NEIL HANLEY

FIRST PUBLISHED IN ISSUE 105 (2012)

The path from aspiring researcher to independent principal investigator is a hard one and, despite promises of ring-fenced cash from research councils to support independent fellowships, many are put off from even applying. Is this pessimism warranted and, if so, what can be done? This account is a personal view of the fellowship system, and how to make it work for you.

We are all familiar with the situation: you are doing well in either clinical or basic science training, getting some papers, some invitations to speak, and helping out on writing grant applications. It's all going well, but how to take the next step to independence? The system that's in place to help involves fellowships. These are offered by a range of funding bodies, research councils, Wellcome, and disease-specific charities. Their objective is to find and fund the researchers of the future. The mantra applied is 'person, place and project'.

PERSON

The level of achievement is dependent on the level of the scheme applied for, and the disease-specific charities may also be looking at the content of the work published to date. The emphasis is on quality rather than quantity, but too many applicants are put off applying for fear their publications are not good enough. In a field such as ours, where the top specialty journals carry an impact factor of less than 6, a balance between top specialty and some supraspecialty articles will buy an entry ticket. Additional marks of esteem include awards, grants and invitations. A background of sustained high-level activity, such as international appointments and collaborations, on a background of excellent undergraduate and postgraduate grades, helps.

PLACE

There is anxiety amongst panel members that established investigators may use fellowships to fund their lab. Therefore, to optimise training, candidates are often encouraged to move, spend some time abroad, and to offer a strong justification for remaining within their current lab environment. The host institution needs to demonstrate a track record and infrastructure to support fellows in transition to independence. Frequent questions to candidates at interview are 'What will be yours at the end of the fellowship?' and 'How does your fellowship project differ from the programme grant held by Professor X?'. Therefore, prospective fellows need to have frank discussions with sponsors/mentors at an early stage to ensure appropriate support.

PROJECT

The project should be ambitious, address a major question, and include clearly defined training components. A project which will require application of several approaches to address the core question will be more attractive than one which is centred only on a single methodology, as this mitigates the risk of things not working out. It is helpful to be explicit in writing who is doing what, and from whom the training/mentorship will come. Areas of overlap between host lab and the fellow can be beneficial, but should be described clearly, and the management of time, effort and resource explained. Fellowship panels have limited breadth of expertise, and rely on expert referees, but typically will require an interview. Therefore, it is very helpful to the non-expert panel members, all of whom will vote, to provide a lucid lay abstract. If they are not interested after reading this then the application is sunk! Summary diagrams, flow charts, and Gantt charts are also very useful.

The interview is the final stage in securing your award. Getting to this stage is the objective of the paperwork. Getting through the interview requires additional preparation. The panel like to see a short, logical and plausible presentation of the topic area to be addressed. After this, an enthusiastic candidate able to answer questions in a clear succinct manner is gratefully received. Good body language is essential: look like you want it! Often the discussion will centre around concerns that the project is not feasible as written, but that with such a strong, enthusiastic candidate the risk of failure is minimised because 'they will find a way to make it work'. Equally, sometimes the panel feel that it is a kindness to prevent a candidate embarking on a research fellowship which they do not fully embrace!

The interview will require serious attention to detail, and should be rehearsed, in front of a naïve panel of critical judges. A chat over coffee with your mentor is NOT useful preparation! If you are invited to speak for 3 minutes about the project, ensure you do just that. Do not overrun, as you will be stopped, and this will throw you off balance and leave a bad impression. Likely questions are easy to guess, and having coherent answers prepared and rehearsed calms the nerves, and contributes to an air of efficient organisation. Try not to ask questions at the end – the panel are unlikely to know the answers, and you leave on a rather awkward note!

DAVID RAY
2006, 2007, 2009 MRC Clinical Training Fellowships Interview Panel

NEIL HANLEY
2012 MRC Clinical Training Fellowships Interview Panel
2007–2011 NIHR Trainees Co-ordinating Centre Postdoctoral Fellowship Panel

TRADE-OFF – BUT ALL IS NOT LOST

I started with good intentions. I wanted to be a doctor: someone who could make people better or, at least, prevent them getting worse.

It was 3 years of clinical training before I qualified in medicine, followed by several standard junior hospital posts over 4 years. I now felt confident that I could take a medical history, perform a general medical examination, postulate a reasonable differential diagnosis, and suggest some of the more pertinent investigations. I had also chosen to pursue a career in hospital medicine rather than general practice. I was proud that I had acquired and developed my clinical skills and, at this point, made the crucial decision to specialise in endocrinology.

I entered the specialty as a research fellow and progressed to become a consultant. Henceforth there was a trade-off. As fast as I learnt about endocrinology, my general medical skills atrophied. It was inevitable and predictable; there were no more attempts to listen to or interpret heart murmurs, whispering pectoriloquy disappeared soundlessly, and rectal examination remained left behind forever. The path was inexorable. Stethoscope now gathering dust, my sole companion in the clinic was my orchidometer.

Over the subsequent 30 years, I remained research-active, associated with an even greater focus on one gland, the pituitary, as opposed to the whole endocrine system. If truth be told, I now even had a favourite hormone. In fairness, it could have been worse, my interests might have been reduced to a sub-unit rather than a whole hormone. The process of deskilling over this time period was relentless; I was aware of the loss of my general medical skills, and a little sad at being confined to so narrow a field as the actions of a single hormone.

Salvation and greater self-respect came from an unlikely source. In retirement I had discovered the existence of ResearchGate, a commercial social networking site for scientists and researchers. I soon realised that it knows an enormous amount, if not everything, about my own research publication history and that of everyone else. In any one week it tells me how many citations or reads of my research publications have occurred, and whether or not the reads are in Bolivia, USA, Japan or anywhere.

> ***'ResearchGate recommends that I consider applying for a post in lung therapeutics, or gynaecology, or microbiome dynamics, or translational kidney physiology, or, even, plant metabolism … no longer do I consider myself a one-trick pony.'***

What really appealed to me about ResearchGate, however, was the 'Jobs you may be interested in' section. After all, ResearchGate knows all my research publication history (even down to book reviews written 30 years ago) and yet, currently, it recommends that I consider applying for a post in CNS/psychiatry, or inflammation, or as group leader in translocation of complex macromolecules across the intestinal epithelial barrier, or translational cardiology, or lung therapeutics, or gynaecology, or microbiome dynamics, or translational kidney physiology, or, even, plant metabolism. What an all-rounder ResearchGate considers me to be!

OK, none of these posts require my whispering pectoriloquy detection gene to be reawakened but, with the support of ResearchGate, no longer do I consider myself a one-trick pony. In a time of crisis, ResearchGate has been good for my mental health.

'HOTSPUR'

OPEN ACCESS: SHOULD JOURNALS BE FREE FOR ALL?

WRITTEN BY STEVE BYFORD

FIRST PUBLISHED IN ISSUE 73 (2004)

Steve Byford examines the issues and asks what would a change to open access mean for science and the Society.

Scholarly literature should be available freely online, with no access restrictions. There's been an increasing amount of talk about this idea, usually called open access, both in the general press and in the scientific literature. Open access journals would be funded instead by charges to authors – or rather their funding bodies. The Society has been considering it carefully for some time, and it continues to be a hot topic.

A recent related development is the Open Archive Initiative, which encourages institutions to set up online repositories for their researchers' papers, which would then be available freely to all. This might not seem an immediate threat to traditional journals, as no one wants to search across many institutions' websites. However, new developments would allow readers to search across many such repositories from special centralised search engines. Why should libraries pay for journal subscriptions if their readers can easily access the same papers for free?

Open access journals have been with us for some time, notably from BioMedCentral, a commercial company, which has charged authors $500 (whilst estimating that its costs are probably four times this). Lately the Public Library of Science (PLoS), originally a pressure group, has become an open access publisher, with *PLoS Biology* and *PLoS Medicine* already launched, and more titles promised. PLoS charges $1,500 per article but admits that this does not cover its costs.

There was recently a bill before the US House of Representatives (the 'Sabo bill') that said 'publicly funded research should be publicly available'. The implication was that the funding for research would cover the costs of publication, but this was not stated explicitly. Perhaps there was a naïve assumption that there would be no costs. Several US newspapers picked up the story and ran articles criticising publishers' outrageous profits, the apparent implication being that all scholarly publishers were equally guilty. Pressure from librarians is also continuing – it is often attributed to the academics they serve, but we've rarely heard from endocrinologists who are passionate about this!

More recently still, the UK House of Commons Select Committee on Science and Technology (to which the Society made a submission) has produced a report including, amongst its 82 conclusions, a recommendation that all UK-funded research output be deposited on free online institutional repositories. In the USA, the National Institutes of Health (NIH) have produced draft proposals that would require all NIH-funded authors to place their final, accepted manuscript on PubMed Central for free access, and for journals publishing the papers to make them freely available no more than 6 months after publication. The publisher Springer has announced an optional author-pays, free-to-reader scheme ('open choice') for its journals. Elsevier now permits authors to deposit their accepted papers on free-to-reader institutional repositories.

What should the Society's view be?

WHAT'S WRONG WITH THE CURRENT SYSTEM?

It's sometimes argued that the subscription model has served the academic community well for decades, producing high-profile quality-assured journals. Why throw that away? Wouldn't it be better to defend it vigorously? The trouble is that it has some deep flaws, leading some to wonder how long it can remain viable.

Perhaps the strongest symptom is the fact that most mature journals lose a small percentage of their library subscribers every year. Since most of the costs of publishing are independent of the number of copies produced, publishers' unit costs increase, which forces up journal prices. This leads to a vicious cycle of further cancellations, since library budgets can't keep up. The underlying cause is not primarily irresponsible pricing by publishers (although not all have been entirely innocent), but the mismatch between the funding for research on the one hand, and the funding for the dissemination of its results on the other. Over the last several decades, the amount of scientific research being done around the world has grown enormously, resulting in more and more research papers, which needed to be published in more or bigger journals. Libraries have not usually been provided with anything like the same proportion of extra money with which to buy them. So the round of cancellations began.

That's not the only problem. The journals market is dysfunctional in other ways. For example, if you were to sit down and compare the prices of journals with their perceived quality, or with their impact factor ranking, you might be in for a shock. We have come across journals from large commercial publishers with prices up to five times that of higher impact, comparably sized direct competitors from not-for-profit learned societies. Why haven't market forces corrected this? It's perhaps largely because of the fact that the decision to publish in a particular journal is divorced from financial factors – librarians know all about prices, and researchers know all about quality ranking. The two issues get pondered in two separate sets of heads.

'It's sometimes argued that the subscription model has served the academic community well for decades, producing high-profile quality-assured journals.'

Are there other solutions? Against a backdrop of restricted purchasing power by libraries, how might the Society seek to disseminate its journals more widely, and still protect its subscription revenue? It's a good question, because we've historically relied on our journals to be a major contributor to funding all the other things we do for the benefit of endocrinology, in fulfilment of our charitable remit. This remains largely the case, even though we've succeeded in developing other revenue streams, via Bioscientifica's growing range of services.

One approach is to find ways of giving a lot more online access (which doesn't cost much to provide) to additional sites that wouldn't have been able to buy additional conventional subscriptions, and to do so for a

comparatively small amount of extra money. This is something that appeals to consortia of universities, for example, only some of whose members currently have an institutional subscription, or to large companies who want online access to their entire corporate network across many sites. Clients get wider access, we get wider dissemination and a little more money – everyone wins!

Well, almost. The trouble is, setting up and maintaining the terms of these deals is a labour-intensive process. Librarians also find it easier to justify their time if they can negotiate for a large number of journals at once, meaning that the large commercial publishers end up with a considerable advantage, not least because they find it easier to send out large, region-specific sales forces. Librarians often end up committing large proportions of their budgets, often over several years, to the very publishers they say over-price for lower quality journals, whilst squeezing the amount that's left for the smaller publishers whose products they say offer better value. It's an odd world.

The Society has tried to combat this by co-operating with other small not-for-profit publishers to offer its journals jointly with theirs. For example, we've recently signed up to one initiative that offers 430 journals from 44 diverse international small publishers. That should make us a bit more noticeable. However, whilst 'multi-site licensing' stands a good chance of alleviating the symptoms of the current problems, it doesn't really address their root cause. It also needs a lot of administrative effort.

HOW COULD OPEN ACCESS HELP?

Immediate freedom of access to scholarly research results is intuitively attractive to us all. As readers, we want ease of access from any location, as authors we want our work to be disseminated as widely as possible. These expectations are frustrated by a system that restricts access to just those journals our own library can afford.

The mismatch between funding for research and for its dissemination could be removed at a stroke if research funding bodies included, as part of their research grants, funds for authors to pay for the publication of their results. The current mismatch between the price and quality of journals would be directly under attack if an author's choice of journal were influenced not only by the journal's perceived prestige and quality but also by the publication costs. Any price differentials would then be transparent to the researcher and the market would force a link between price and quality.

Under the new model, publishers would sell a service to authors. They would be judged by the extent to which they maximised the exposure and credibility of the work they published, and by how much added value they gave the work compared with authors merely depositing their manuscripts on their institutions' online repositories.

The Society has been enthusiastic about the principle of an open access model for some time. As far back as 1999 we were suggesting that the research grant, rather than the library budget, would be a better funding route for research dissemination, for precisely the reasons outlined above.

WHY DELAY? OPEN ACCESS TODAY!

Well then, what's to stop us embracing the new model? It's perhaps obvious that it won't work for every kind of journal: what about clinical research for which there is no grant? Similarly, it's difficult to see how review journals could be financed this way. Even so, what's to stop us switching our basic science research journals over to open access? How do we make the transition?

> ***'It's as though an open access paradise is visible to us in the distance, but in order to get there we have to cross a bottomless ravine using an unsafe rope bridge.'***

There's the rub. A promising route that captured the Society's imagination was the so-called 'hybrid transition model'. Charge the authors an optional fee: if they choose to pay, their article becomes free to all; if not, it's restricted to subscribers, as at present. That looked as though it might take us forward while limiting the risks.

That's until you project the money we might get. Our financial viability then turns out to depend precariously on a few key parameters. First, how much should we charge authors? Then, what proportion of authors would take it up? Finally, how would this affect our subscription income? The answer to the first affects the second, which in turn affects the third. Set the price too low and we won't get enough money to cover our costs, and we encourage a high level of take up. If that means a substantial fraction of the journal is free, many librarians will heave a sigh of relief and cancel their subscription. Under certain, very plausible scenarios, that could kill the journal that tries it. Set the author fee at a more realistic level and it will be perceived as extortionate, and we lose the sympathy and loyalty of our authors and readers.

It's quite scary. Tweak these parameters by not a lot, and the Society could either be rolling in extra cash or, quite simply, permanently out of business. Worse still, because the effects on subscriptions would not be immediate, it could be 2 or 3 years before a fatal decision took its toll – we wouldn't know until then what its effect had been.

And that's frustrating. We have here a new model that could solve everything, but which could destroy everything as we edge towards it. It's as though an open access paradise is visible to us in the distance, but in order to get there we have to cross a bottomless ravine using an unsafe rope bridge.

That's unless we can find another way over. Can we launch an open access experiment without serious risk to our financial viability? This is exercising our minds greatly at the moment. Meanwhile, your Council and Publications Committee would be extremely interested to hear your views! And then, as they say, watch this space…

STEVE BYFORD
Publications Director, Society for Endocrinology
(correct at the time of first publication)

ENDOCRINE CONNECTIONS
THE FUTURE OF ENDOCRINE PUBLISHING

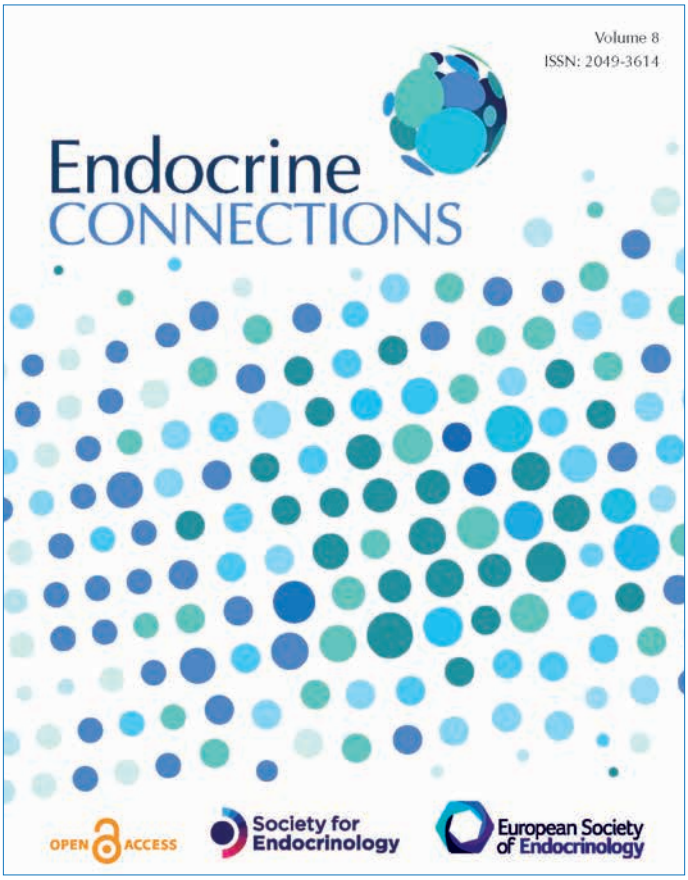
Adrian J L Clark became Editor-in-Chief of the Society's open access journal *Endocrine Connections* in January 2021. Here, he shares his thoughts on why open access is fundamentally important to the future of journal publishing.

The internet has radically changed so much in our lives over the last two or three decades, and scholarly publishing is no exception. In some respects, however, the changes in publishing have been slow.

The most obvious influence of the internet is in the ability to search for publications in one's area of interest from a laptop or phone, rather than trekking over to the institutional library and scrolling through massive tomes such as *Indexus Medicus*, or writing down citations from other papers and then hoping that the library holds the journal you need and that the relevant volume and issue is on the shelves – frequently not the case, in my experience.

Now you can identify relevant and recent publications in a non-prejudicial way within minutes. This is a massive advance on the pre-internet struggle.

Unfortunately, accessing those papers can often falter at this point. Although you can see the abstract from your computer, you frequently cannot obtain the paper unless your institution happens to subscribe to that journal, or you or your institution is willing to pay extravagant sums to purchase a reprint.



Institutional libraries are under growing financial constraints, and there is a roughly 10% annual decline in subscriptions to scholarly publications at present. Consequently, I believe that, with the exception of a handful of the top 'coffee table' journals, the traditional print journal and the annual journal subscription model is now facing serious decline.

The solution is open access publishing. Much of the research we publish has been supported in one form or another by public bodies: either government bodies (including the NHS and universities) or charitable organisations. Not surprisingly, they have no interest in the research they fund being limited in its distribution. Consequently, most UK and European funders will mandate that you publish open access. Add to this the fact that open access publications are downloaded and cited significantly more than 'pay per view' papers. One major publisher reports that an open access publication will attract four times more downloads and 1.6 times more citations than traditional papers, making this form of publishing a 'no brainer'.

'An open access publication will attract four times more downloads and 1.6 times more citations than traditional papers, making this form of publishing a "no brainer".'

Almost a decade ago, the Society for Endocrinology, the European Society of Endocrinology and Bioscientifica saw this trend coming and launched a new endocrine journal: *Endocrine Connections*. They realised that a further benefit of internet searching and open access was that there was no advantage in launching a highly specialised journal. Consequently, this presented the opportunity to develop cross-disciplinary 'connections' within endocrine science and beyond. Now widely indexed, and with a respectable impact factor, thanks to the efforts of its two former Editors-in-Chief, Jens Sandahl Christiansen and (following Jens' untimely death) Josef Köhrle, *Endocrine Connections* has come of age.

The drawback to open access publishing in many authors' minds is the cost of the 'article processing charge' (APC), which is intended to compensate the publisher for the loss of income resulting from not owning the copyright to the article. Certainly, with some top of the range journals, the APCs are eye-wateringly large (indicating how profitable it is for them to publish your work and retain the copyright). It is notable that *Endocrine Connections* has one of the lowest APCs amongst the endocrine journals and, as a Society member, you pay a substantially reduced rate. Of course, when you publish open access, you retain the copyright and can copy, distribute, transmit and adapt the work for commercial or other purposes, provided the work is properly attributed – something that should be encouraged.

As should be well known, the profits from all Bioscientifica journals go entirely to support their parent societies, so members see the benefits of APCs in the form of meetings, travel grants and other awards, and publications such as the one you are now reading.

ADRIAN J L CLARK
Editor-in-Chief, *Endocrine Connections*
Emeritus Professor of Endocrinology, St George's University of London and Honorary Professor of Endocrinology, Barts & the London, Queen Mary University of London

Endocrine CONNECTIONS

European Society of Endocrinology

Society for Endocrinology

Find out why you should make *Endocrine Connections* the home of your next publication

The official open access journal of the European Society of Endocrinology and the Society for Endocrinology *Endocrine Connections* publishes basic, translational and clinical research and reviews in all areas of endocrinology in order to further research, education and clinical practice in the field.

1 2.592

Impact Factor

Latest Impact Factor is 2.592
(Five year score is 2.822)

2

Fully open access

Offering authors the highest possible visibility for their work and stimulating cross-discipline collaboration in the areas of basic, translational and clinical research and reviews

3

Global audience

Over 285,000 yearly readers

4 40% OFF

Highly competitive costs

a 40% discount on Article Processing Charge for European Society of Endocrinology and Society for Endocrinology members

5

Rapid peer review and publication

Our average response time from submission is less than 4 weeks

6

International Editorial Board

Led by Professor Adrian Clark

7

Owned by ESE and SfE

Have your research backed by two of the largest endocrine societies in the world, the European Society of Endocrinology and the Society for Endocrinology

8

International public exposure

High impact articles are promoted to news outlets via our press team

9

Stringent data quality

Our dedicated statistical advisor is committed to ensuring only the highest quality data and methodologies are accepted

10 26

Indexed in 26 locations

Including PubMed, Google Scholar, Scopus and Altmetric

Submit your next article at
ec.bioscientifica.com

published by bioscientifica

follow us on Twitter @EndoConnect

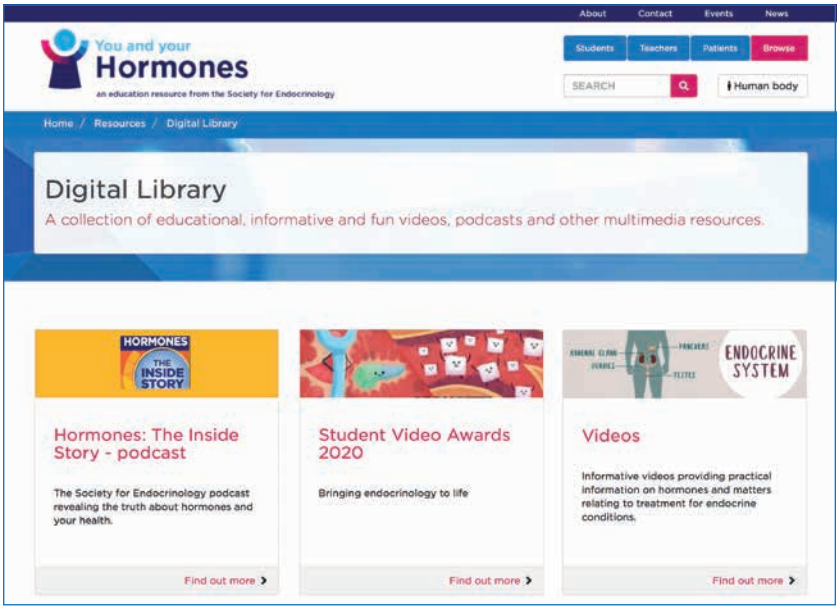
Green tick of approval in schools
FOR YOU & YOUR HORMONES

The Society's public-facing educational resource, You & Your Hormones, has been awarded an Association for Science Education (ASE) Green Tick. This certification means that You & Your Hormones will now be promoted as an ASE-evaluated resource that can support learning about hormones in schools.

BUILDING ON SUCCESS

Since its launch in 2011, You & Your Hormones has always aimed to provide the latest information on hormones and hormone-related conditions to the general public, including patients and students. Back in 2015, the site averaged just over 25,000 visitors per month. This has since exploded to over 112,000 users per month in 2019. Its excellent search engine index ranking means most visitors arrive via search engines when researching hormones or endocrine-related topics.

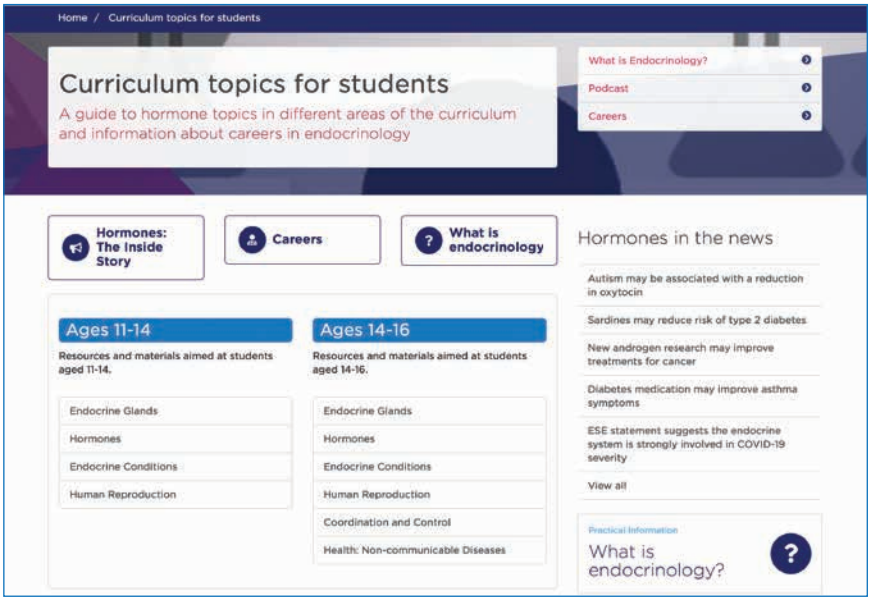
This fantastic progress aligns with our charitable aim of engaging the public with endocrinology and its impact. It shows great momentum in the fight against the plethora of hormone misinformation that can be found online.



Digital library Our new image-led collection of multimedia resources provides easy access to episodes and transcripts from our podcast series 'Hormones: The Inside Story'. The excellent 2020 Student Video Award winners and our own 'What is endocrinology?' videos are now easy to find and the collections are ready to be expanded.

Over **2.7 MILLION** YYH page views in 2020

Curriculum topics All relevant curriculum resources are now categorised by topic and age, for easy access.



BECOME A CONTENT EDITOR

Are you a scientist, clinician or nurse, passionate about endocrinology?

Boost your writing and public engagement skills whilst promoting accurate and reliable science by applying to join the You & Your Hormones team.

Find out more and apply at **www.endocrinology.org/outreach/content-editors**

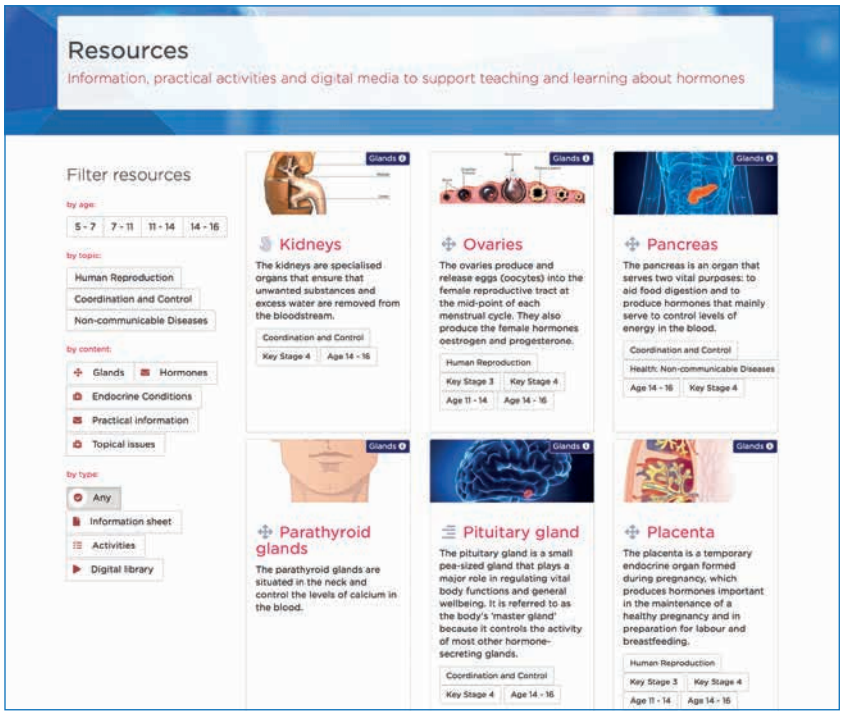
WWW.ASE.ORG.UK

You and your Hormones

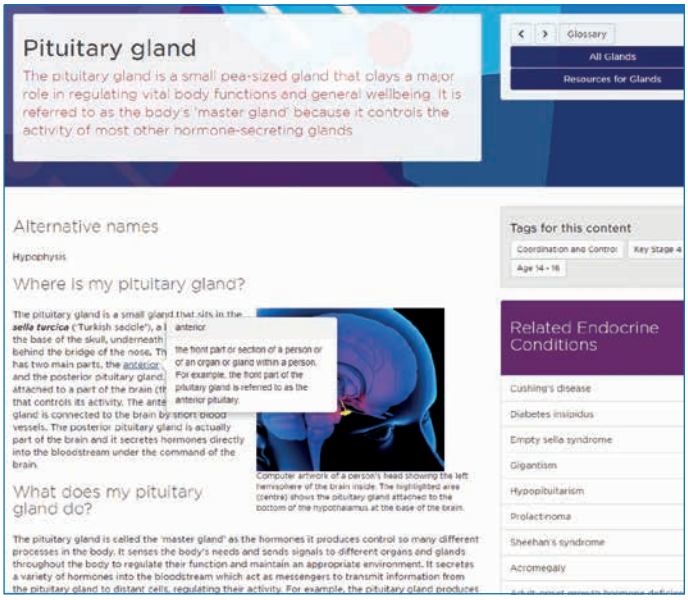
WWW.YOURHORMONES.INFO

TARGETING SCHOOLS

An entire section of the site is dedicated to students and teachers. These are key audiences, but our access to them is limited through our established communication channels. As part of the Society's continuing mission to promote accurate knowledge about hormones, our Public Engagement Committee and the You & Your Hormones Editorial Board have been working hard towards improving the website's appeal as an educational resource for schools. This has culminated in several facelifts to the site, and has driven the creation and curation of more engaging and digestible digital resources to help meet the criteria of the ASE Green Tick Certification Scheme. These updates have produced a more easily searchable, smoothly navigable, mobile-friendly, image-driven website for school teachers and students.



Resource filtering In addition to student age and curriculum topic, results can be filtered by content category and type of resource, to further enhance the site's usability.



Glossary New behind-the-scenes features simplify navigation of the site:

1. Search function adjustment now allows misspellings and non-exact phrasing to return the correct results.
2. 'Popover' glossary summaries on keywords in articles aid comprehension without interrupting the readers' flow.
3. Site functionality has been optimised for speed, mobile phone viewing and search engine rankings.

WHAT DOES THIS MEAN?

The ASE Green Tick Certification allows us to refocus the delivery of our existing content and contribute to the overarching mission to increase engagement with school teachers and school children. It positions the site as a tool for understanding hormone science. You & Your Hormones' huge amount of valuable, expert information is now easier to access, with curriculum-relevant pages and resources now clearly tagged to increase usability for teachers and students.

Of course, this is a work in progress, and our future plans intend to expand upon the range of multimedia resources, educational tools and up-to-date information on hormones and hormone health.

As Society members, please encourage your colleagues, friends and school contacts to use the site as their first port of call for authoritative, expert and engaging information about hormones.

- Do you have **resources** that could be used to teach students about hormones?
- Would you like to join the **content editing** team?
- Do you have any **feedback** on the new look or suggestions for the Editorial Board?

Get in touch with **media@endocrinology.org**

Defining the FUTURE OF ENDOCRINOLOGY

The onset of the COVID-19 pandemic in 2020 was a watershed moment that resulted in completely new ways of working. It also provided a point in time to reflect on current clinical service models and their need for radical change, including better use of digital services, new service models, streamlined referral and better integration with primary care. It gave an opportunity to innovate and create services fit for the future: ones that are truly patient-centred.

At the same time, significant challenges became immediately apparent, not least of which was how, in this new world, was training in endocrinology going to be achieved and made fit for purpose?

At an extraordinary meeting of the Society's Council on 15 May 2020, the decision was made to be at the forefront of this potential transformation, and the formation of a new working group was approved. Reporting to the Clinical Committee, this group would consider and relay opportunities to reshape clinical care and delivery of training in endocrinology across the UK. Its mission would be 'to transform clinical care, bringing together UK-wide expertise across clinical endocrinology to define the most effective, future focused endocrinology service models and recommend how these are best implemented and sustained within the NHS post-COVID-19'.

WORKING GROUP MEMBERSHIP

An open call was put to the membership to join the group, asking for specific examples of skills and experience. This call saw a large number of members volunteering to be involved, with consultant, endocrine trainee, specialist nurse and pharmacy and GP representation being recruited. Ahead of the first meeting, all affiliated patient support groups were asked for input regarding what 'good' would look like for their community, and to suggest examples of ways in which services could be improved. Their input informed discussions at the first meeting.

A further subset of applicants who had specialist expertise were invited to become affiliated members of the working group, including representatives of all the devolved nations, and the remainder were asked to act as initial consultants as the work of the group progressed.

PROGRAMME OF WORK

All discussions took account of the detailed work that had taken place as part of the GIRFT (Getting It Right First Time) visits and report (led by John Wass), the NHS long term plan and the direction of travel as guided by the CRG (Clinical Reference Group) for Specialised Endocrine Services (chaired by Neil Gittoes).

We set ambitious timelines to complete the work by the end of 2020, but we were naïve and had not foreseen the degree to which the COVID second wave would affect us all. Planning for that second wave was the first priority and by October 2020 that key work package was delivered, with advice and resources published on the Society's website. These recommendations will apply if we experience a third COVID wave.

With the second wave easing, the group is back up to full speed and working hard on the two remaining significant work packages. These are focused on the curation and sharing of resources and tools, using examples of best practice and innovation to improve the patient journey. They can be used and adapted by the endocrine community in the UK. The overall aim is to support a framework that ensures the right care at the right time and at the right place, innovatively placing the patient/patient record at the centre.

Read the recommendations for the COVID-19 second wave at **www.endocrinology.org/2ndwave**

CORE WORKING GROUP MEMBERS

Consultants
- **KRISTIEN BOELAERT Co-chair** (Birmingham)
- **JOHN NEWELL-PRICE Co-chair** (Sheffield)
- **AFROZE ABBAS** (Leeds)
- **ANTONIA BROOKE** (Exeter)
- **MARALYN DRUCE** (Barts)
- **HELENA GLEESON** (Birmingham)
- **STEVEN HUNTER** (Belfast)
- **ASHWIN JOSHI** (Sunderland)
- **CHRISTINE MAY** (Oxford)
- **KARIM MEERAN** (London)
- **DOUGLAS ROBERTSON** (Mid-Cheshire)
- **HELEN SIMPSON** (London)

Trainees
- **SHAZIA HUSSAIN** (Royal London Hospital, Barts)
- **KATE LAYCOCK** (Homerton and Barts)

Nursing
- **SHERWIN CRISENO** (Birmingham)

ADDITIONAL NON-SOCIETY MEMBERS

Primary care
- **CLARE HAMBLING** (Norfolk)
- **HELEN PARRETTI** (East Anglia – representing the RCGP)

Pharmacy
- **PHILIP NEWLAND-JONES** (Southampton)

Key areas include:
- Education and training
- Primary care interface
- Digital care options and models of care (including patient self-care)
- Focused endocrine disease-specific models of care

The two further outputs from the group will be:
- Output 2: Resource Hub – this will reside within the Members' Area of the Society's website and will continue to grow and develop, providing members with a live repository to share ongoing areas of good practice beyond the completion of the working group.
- Output 3: Report of recommendations (with member/stakeholder consultation pre-publication) and suggestions for further developments.

The group is set to complete its main work around the end of June 2021, with member and stakeholder consultation taking place in July and August, and a final report for Council in September. There will be a further presentation at the Society for Endocrinology BES conference in November. Your input into all of this is needed, so please share your opinions during the consultation phase.

Huge thanks must be extended to the core members of the working group for tireless work on this project, especially during the pandemic. The work has only been possible because of superb support from Society staff: Zoe Plummer, Laura Udakis and Sarah Don-Bramah.

JOHN NEWELL-PRICE
KRISTIEN BOELAERT
Co-Chairs, Future of Endocrinology working group

Strengthening member representation: AN UPDATE ON OUR GOVERNANCE REVIEW

In July 2020, Council agreed to conduct a review of the Society for Endocrinology's governance, including the structure of Council and the Committees and other decision-making groups, the breadth of expertise represented and the underpinning processes involved in the running of the Society.

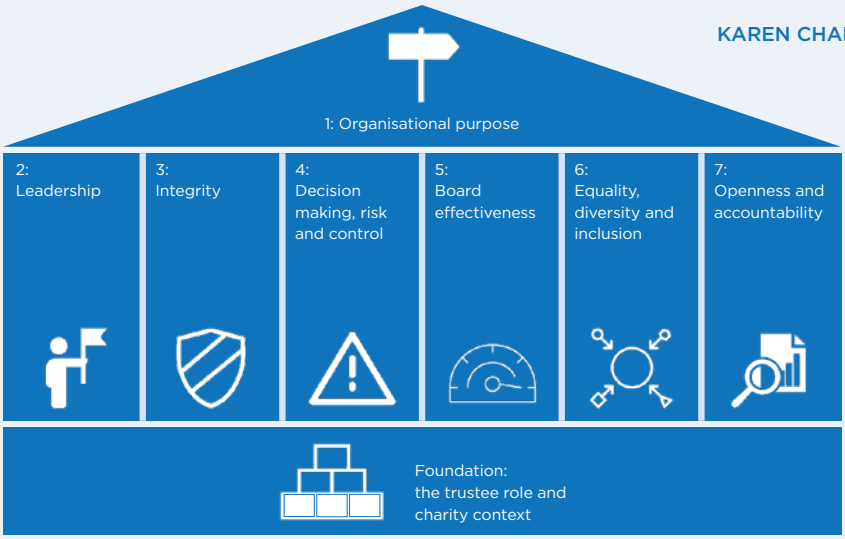
Importantly, this review was not commissioned to address a particular problem or set of issues, but rather to ensure our Society is fit and well-equipped to serve its members and champion the field of endocrinology in the most impactful way into the future. The field of endocrinology is incredibly broad, and our Society must represent a diverse community that spans the scientific–clinical spectrum. We must, therefore, continually work hard, in order to meet the challenge of representing the voices of all the members we serve, if we are to satisfy our charitable aims (see panel).

Following my appointment by Council as Chair for the review, an open call was put to the membership to recruit a working group to oversee the review process. The participants in the group (see below) were chosen based on their interests and experience in governance and, as far as possible, to represent the breadth of the membership. Only two members of the group were currently serving on any of the Society's Committees, though several had done so in the past.

Three subgroups were set up to explore particular areas in more detail – leadership, decision making, and equality, diversity and inclusion – with their outputs brought back to the working group for discussion and agreement.

The working group used the Charity Governance Code as a framework for the review and considered the Society's performance against its seven areas, listed in the figure. The recommendations of the group were reviewed by our external governance consultant and refined with the benefit of her expertise.

To inform the conversations of the working group, I held a total of 22 interviews with members who were currently serving (or had previously held positions) within the Society's governance structure, and who represented a range of member categories and backgrounds. In addition, a survey was distributed to all Committee members, over a 2-week period, to gather views on Committee effectiveness.



OUR CHARITABLE AIMS

- To advance scientific and clinical education and research in endocrinology for the public benefit
- To attract high quality scientists, doctors and nurses into endocrinology and support their professional development to advance science and medicine
- To engage the public with endocrinology and its impact
- To raise the profile and be the voice of endocrinology in the UK
- To promote and support the global endocrine community through collaboration

Four main themes have begun to emerge from these consultations, as areas for development:

1. Better representation of members and their interests across all areas of practice, both clinical and scientific, as well as meeting societal needs; and the role of the Endocrine Networks within the governance process
2. More inclusive election processes to foster better member engagement and diversity with the governance of the Society at all levels
3. Focusing on the future generation and ensuring that early career members have more of a voice in the Society's decision making
4. Education and training.

An initial report and set of recommendations were taken before Council at the end of May 2021 at an Extraordinary Meeting. Following this, all members will be able to express their views on this report through a consultation process during June 2021. A final report and recommendations will go back to Council then before a clear and robust plan is put in place to implement the recommendations.

You can find details of how to get involved at **www.endocrinology.org/about-us/governance/society-governance-review**.

KAREN CHAPMAN

WORKING GROUP MEMBERS

- **PROFESSOR KAREN CHAPMAN** Scientist (Edinburgh) (Chair)
- **PROFESSOR TIM COLE** Scientist (Melbourne, Australia)
- **PROFESSOR HILARY CRITCHLEY** Clinical Academic (Edinburgh)
- **MS CHONA FELICIANO** Nurse (Birmingham)
- **DR ANNEKE GRAF** Early Career Clinician (London)
- **DR STEVE ORME** Clinician (Leeds)
- **DR JESSICA PIASECKI** Early Career Scientist (Nottingham)
- **DR DOUG ROBERTSON** Clinician (Cheshire)
- **PROFESSOR CLAIRE STEWART** Scientist (Liverpool)
- **PROFESSOR JEREMY TOMLINSON** Clinical Academic (Oxford)

A FORGOTTEN PIONEER OF ENDOCRINOLOGY IN BRITAIN: WHO WAS MRS BISBEE?

WRITTEN BY MALCOLM PEAKER

Mrs Bisbee was the author of no papers on endocrinology, but yet she was the mentor of pioneering endocrinologists, founders of *Journal of Endocrinology* and stalwarts of this Society who, in turn, propagated the subject in many parts of the world.

THE BEST LECTURER EVER ENCOUNTERED

I first heard of this lecturer at the University of Liverpool from John Phillips (Chairman of the Society for Endocrinology, 1981–1984) and Alan Wright (both Liverpool graduates) in Hong Kong in 1966. I remember the line, '… she started everybody off'. Only recently have I uncovered just who some of the 'everybody' were, and something of her sad private life.

Readers of Lord Zuckerman's autobiography *From Apes to Warlords 1904–46*[1] cannot fail to notice his praise of Mrs Bisbee, who was seconded to the University of Cape Town in 1924. He commented on her inspirational lectures and her encouragement of his research on reproduction in baboons. That led directly to his work in London and, in turn, to the launch of *Journal of Endocrinology* in 1939 (which Zuckerman edited for many years) and the Society for Endocrinology in 1946.

At Liverpool in the 1930s, Mrs Bisbee supervised postgraduate students in research on endocrinological topics that she initiated. 'Harry' Waring (1910–1980), who went on to become the doyen of environmental physiology and endocrinology in Western Australia, did seminal work on the mouse adrenal. He noted that she suggested the topic while helping and criticising throughout. Similarly, in his biographical memoir for the Royal Society, James 'Jimmie' Munro Dodd (1915–1986) records his indebtedness to her for getting him interested in comparative endocrinology. He described her as quite the best lecturer he ever encountered. Ian Chester Jones (1916–1986) (Dale Medallist in 1976 and former Secretary of the Society for Endocrinology) was also steered to work, like Waring, on the mouse adrenal.

The importance of Mrs Bisbee in fostering endocrinology in its early days is clear. But who was this 'remarkable lecturer'? With the help of genealogical search sites, old newspapers and material in the archives of the University of Liverpool, I have found something about her, as well as the tribulations of being a female university scientist in Britain in the first half of the 20th century.

A WOMAN IN 20TH CENTURY SCIENCE

Ruth Culshaw Bamber, the daughter of a gamekeeper, was born on 30 November 1889 near Ormskirk in Lancashire, UK. She graduated from Liverpool with first class honours in 1913, followed by an MSc in 1914. She was appointed lecturer in 1915. In 1919, her life changed, but not in the way she expected. She had met an American, George Allen Bisbee, who was working for the YMCA in Liverpool near the end of the First World War. In 1919, she sailed to New York where they were married on the day the ship arrived. However, something must have gone wrong because instead of living in Pittsburgh, as was her intention, she sailed back to Liverpool 2 weeks later.

The marriage was annulled sometime in the early 1920s. However, she had become a US citizen by dint of marriage and, in 1924, had to apply for renaturalisation. Her travails did not end there. She had not told the university of the annulment (an unmentionable subject at the time) and when, in 1933, the university decided that all married women must resign and re-apply for a post, she was included in that edict, which is remarkable to 21st century eyes.

She did as instructed, but withdrew her resignation when her true status was revealed. The whole affair became a cause célèbre for women's employment and the university was forced to reverse its policy in 1934. The vice-chancellor responsible for the policy sailed on to become Principal of Glasgow University with a knighthood.

> ***'Mrs Bisbee's scientific children, grandchildren and great-grandchildren spread throughout the world. They have served the Society for Endocrinology as officers and editors.'***

Her personal research (after 1919 always published using the style 'Ruth C Bamber (Mrs Bisbee)') ranged from marine biology to genetics. She became well known for her work on coat colour in cats. From papers in which she is acknowledged for having the idea for a student's research project (no just adding a supervisor's name to a paper then), her confidence in matters endocrinological must have been sufficient in the early 1930s to launch students into the field.

Ruth Culshaw Bamber (Mrs Bisbee) retired, still a lecturer, in 1955. She died on 7 January 1970, aged 80, near Kendal in the English Lake District.

Mrs Bisbee's scientific children, grandchildren and great-grandchildren spread throughout the world, from Hong Kong in the east to California in the west. They have served the Society for Endocrinology as officers and editors.

Perhaps we should do more to commemorate her as the foster mother of the science of endocrinology in Britain.

MALCOLM PEAKER

Malcolm Peaker FRS was Director of the Hannah Research Institute until he retired in 2003.

REFERENCE

1. Zuckerman S 1978 *From Apes to Warlords 1904–46*. London, UK: Hamish Hamilton Ltd.

Despite his best efforts, Malcolm Peaker has been unable to track down an archive photograph of Ruth C Bamber/Mrs Bisbee. If you can help, Malcolm would be delighted to hear from you at **malcolm.peaker@icloud.com**.

THE FIRST 'ENDOCRINOLOGIST'

FIRST PUBLISHED IN ISSUE 75 (2005)

We take a look at the man behind hormones, and celebrate the dawn of British – and international – endocrinology.

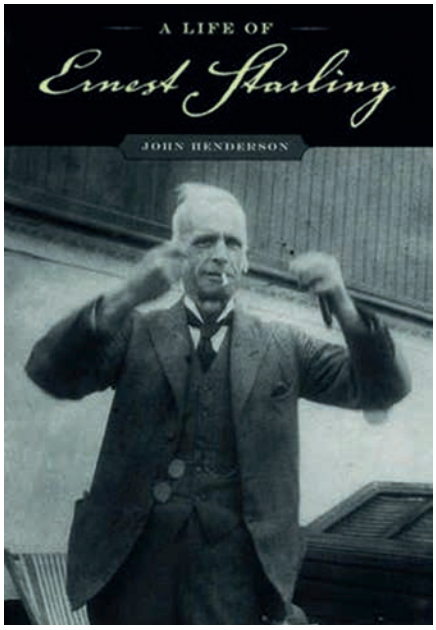
Ernest Starling was born in 1866, and became a key figure in the flowering of British physiology that began around 1885. If a single cause for this flowering can be suggested, it is William Sharpey, who was made Professor of Anatomy and Physiology at University College London (UCL) in 1836. He inspired a generation of physiologists, including John Burdon Sanderson, Michael Foster and Edward Schäfer, each of whom succeeded Sharpey at UCL, before moving elsewhere. Ernest Starling replaced Schäfer in 1899, and stayed at UCL until his death in 1927.

Starling's research covered an extraordinarily wide range of subjects, in a way that would not be possible today. With William Bayliss (who married Starling's beautiful sister Gertrude), he investigated the electrical activity of the heart. They produced the second ever recording of the human ECG. In the late 1890s, Starling investigated the formation of lymph, and showed that plasma osmotic pressure balanced hydrostatic pressure in the capillary ('Starling's principle').

With Bayliss he discovered secretin (1902), and in 1905 he rather casually introduced the word 'hormone' into the language. His heart–lung preparation led to his 'law of the heart' (1913–1914). After the Great War he published – notably – on the kidney (with Verney), and – not so notably – on insulin and the control of blood pressure.

But he was much more than a gifted scientist. He wrote iconoclastically on the English educational system, on Germany and German science, on medical education, on the Government and the Great War (a particularly scathing attack) and the organisation of London University.

He canvassed fruitlessly for the merging of London's medical schools in 1909 (this campaign brought him a good deal of unpopularity). It was not until 1980 that the Flowers Report reduced the number of schools from twelve to five, as Starling had proposed! He was the driving force behind the new preclinical school for UCL, and his Institute of Physiology (1909) was built with £16,000 largely raised by his talented wife Florence. His outspoken views on the Government probably prevented him from being awarded a knighthood, and his admiration for Germany was instrumental in his not receiving a Nobel Prize.



Having spent some years on a biography of this physiological lion, I feel that 2005, the centenary of his term 'hormone', seems an appropriate time for its publication. I hope that I have conveyed in the book something of the Victorian/Edwardian flavour of his world, a world that was bursting at the seams. We shall not see his like again.

A Life of Ernest Starling *by John Henderson was published in 2005 by Oxford University Press.*

FOLLOW YOUR NETWORKS ON TWITTER

Each of our eight Endocrine Networks now has its own Twitter account, run by the convenors. Follow them to share news, events and resources, and to keep up to date with your Network colleagues.

The Endocrine Networks are a platform for collaboration between basic and clinical researchers, clinical endocrinologists and endocrine nurses.

Go to the Members' Area on the Society website to select and update your preferred Networks.

Adrenal and Cardiovascular @adrenalnetwork
Dr Scott MacKenzie & Dr Mick O'Reilly

Bone and Calcium @bonenetwork
Professor Jeremy Turner & Dr Caroline Gorvin

Endocrine Cancer @EndocrineCancer
Dr Ruth Casey & Dr Kate Lines

Endocrine Consequences of Living with and Beyond Cancer @EndoLWBC
Dr Helen Simpson & Dr Claire Higham

Metabolic and Obesity @MetabolicNW
Professor Shareen Forbes & Dr Gavin Bewick

Neuroendocrinology @NeuroEndoNW
Dr Niki Karavitaki & Dr Craig Beall

Reproductive Endocrinology and Biology @ReproNetwork
Dr Kim Jonas & Professor Colin Duncan

Thyroid @Thyroid_Network
Dr Fraser Gibb & Dr Peter Taylor

To contact HRA Pharma Rare Diseases in the UK & Ireland email med.info.uk@hra-pharma.com or call 0800 917 9548.

Date of preparation: November 2020 UK/ENDO/0089